Proposed Registration Decision PRD2010-02

Acetamiprid

(publié aussi en français)

8 February 2010

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6605C
Ottawa, Ontario
K1A 0K9

Internet: pmra.publications@hc-sc.gc.ca
healthcanada.gc.ca/pmra
Facsimile: 613-736-3758
Information Service:
1-800-267-6315 or 613-736-3799
pmra.infoserv@hc-sc.gc.ca

Canada

HC Pub: 091208

ISBN: 978-1-100-14564-8 978-1-100-14565-5
Catalogue number: H113-9/2010-2E H113-9/2010-2E-PDF

Table of Contents

Overview

Proposed Registration Decision for Acetamiprid

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Acetamiprid Technical Insecticide, Assail 70 WP Insecticide, Tristar 70 WSP Insecticide, Acetamiprid RTU Insecticide, and Vault 50 FS Insecticide Seed Treatment containing the technical grade active ingredient acetamiprid to control a variety of insect pests in various fruit, vegetable, ornamental and oilseed crops.

Acetamiprid Technical Insecticide (Registration Number 27125), Assail 70 WP Insecticide (Registration Number 27128; previously known as Assail Brand 70 WP Insecticide), Tristar 70 WSP Insecticide (Registration Number 27127; previously known as Chipco Brand Tristar 70 WSP Insecticide), Acetamiprid RTU Insecticide (Registration Number 27126; previously known as Pristine Brand RTU Insecticide), and Vault 50 FS Insecticide Seed Treatment (Registration Number 28119) are conditionally registered in Canada. The detailed review for Acetamiprid Technical Insecticide, Assail 70 WP Insecticide, Tristar 70 WSP Insecticide, and Acetamiprid RTU Insecticide can be found in Regulatory Note REG2002-05, *Acetamiprid, Assail Brand 70 WP Insecticide, Chipco Brand Tristar 70 WSP Insecticide and Pristine Brand RTU Insecticide*. Subsequent to the original applications, an application to register Vault 50 FS Insecticide Seed Treatment was reviewed and conditionally approved. The current applications were submitted to convert Acetamiprid Technical Insecticide, Assail 70 WP Insecticide, Tristar 70 WSP Insecticide, Acetamiprid RTU Insecticide and Vault 50 FS Insecticide Seed Treatment from conditional registration to full registration.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of Acetamiprid Technical Insecticide, Assail 70 WP Insecticide, Tristar 70 WSP Insecticide, Acetamiprid RTU Insecticide and Vault 50 FS Insecticide Seed Treatment.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (such as children) as well as organisms in the environment (such as those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

Before making a final registration decision on acetamiprid, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Registration Decision on acetamiprid, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document.

What Is Acetamiprid?

Acetamiprid is a neonicotinoid insecticide that is active against insects on contact as well as through ingestion, and it is distributed systemically within plants. End-use products containing acetamiprid are registered for use on a variety of food crops and ornamentals by conventional ground application and for use as a seed treatment on canola and mustard seed.

---

1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act* "...the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's *(a)* efficacy; *(b)* effect on host organisms in connection with which it is intended to be used; and *(c)* health, safety and environmental benefits and social and economic impact".

Health Considerations

Can Approved Uses of Acetamiprid Affect Human Health?

Acetamiprid is unlikely to affect your health when used according to label directions.

Exposure to acetamiprid may occur through diet (food and water) or when handling and applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when using acetamiprid products according to label directions.

The technical grade active ingredient acetamiprid showed high acute toxicity to rats when ingested. Consequently, the statement "Danger Poison" is required on the label for the technical grade active ingredient. The end-use products Assail 70 WP Insecticide and Tristar 70 WSP Insecticide caused moderate acute toxicity in animals when ingested. Consequently, the statement "Warning Poison" is required on the labels for these end-use products.

Acetamiprid does not cause cancer in animals and does not damage genetic material such as DNA. Health effects in animals given daily doses of acetamiprid over long periods of time included generalized toxicity manifested as effects on body weight and food consumption, as well as mild, non-adverse effects on the liver as it adapted to an increased demand to metabolize acetamiprid.

Acetamiprid does not cause birth defects in animals. There was evidence in animals that the young are more sensitive to the effects of acetamiprid than adults. Effects on the young animal were considered more serious than those observed in parental animals at the same dose level. In addition, signs suggestive of neurotoxicity were observed in young animals at doses lower than those that caused effects in parental animals.

The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing infants). Only those uses where exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Residues in Water and Food

Dietary risks from food and water are not of concern

Aggregate dietary intake estimates (food plus water) revealed that children less than two years of age—the subpopulation which would ingest the most acetamiprid relative to body weight—are expected to be exposed to less than 8.4% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from acetamiprid is not of concern for all population sub-groups. A cancer potency factor (Q_1^*) has not been established for acetamiprid. Therefore, a cancer dietary risk assessment is not required.

An aggregate (food plus water) dietary intake estimate for the highest exposed population (children one to two years old) used less than 95% of the acute reference dose, which is below the level of concern. Therefore, the acute dietary risk from acetamiprid is below the level of concern for all population sub-groups.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Confirmatory residue trials conducted throughout Canada using acetamiprid on leafy vegetables, cole crops, field tomatoes, pome fruit and grapes were acceptable. MRLs will not be revised as a result of this evaluation. As such, please refer to the MRL table for this active ingredient on the Health Canada website.

Risks in Residential and Other Non-Occupational Environments

All uses currently registered for the domestic ready-to-use product are not of concern, and entry by the public into treated commercial areas is considered acceptable.

Exposure of the general population to residues of acetamiprid from orchards treated with Assail 70 WP Insecticide could occur by participating in pick-your-own (U-pick) activities for apples and pears. The exposure from such activities were considered acceptable for adults, youths, and children.

Exposure could also occur from homeowners spraying Acetamiprid RTU Insecticide, and subsequently re-entering treated residential areas. Both the use and postapplication exposures to adults, youth and children were considered acceptable.

Occupational Risks From Handling Assail 70 WP Insecticide, Tristar 70 WSP Insecticide and Vault 50 FS Insecticide Seed Treatment

Occupational risks are not of concern when Assail 70 WP Insecticide, Tristar 70WSP Insecticide and Vault 50 FS Insecticide Seed Treatment are used according to the proposed label directions, which include protective measures.

Farmers and custom applicators who mix, load or apply Assail 70 WP Insecticide, Tristar 70 WSP Insecticide and Vault 50 FS Insecticide Seed Treatment as well as field workers re-entering treated fields, nurseries, greenhouses, shadehouses and lathhouses can come in direct contact with acetamiprid residues on the skin, or by inhalation. Therefore, the labels specify that anyone mixing, loading and applying these products must wear: a long-sleeved-shirt, long pants, socks and shoes, and chemical-resistant gloves. In addition, depending on the product, workers may require chemical-resistant coveralls and/or a respirator. The labels also require that workers do not enter treated fields or other treated sites for at least 12 hours after application, or longer, depending on the tasks to be performed. Taking into consideration these label statements, the number of applications and the expectation of the exposure period for handlers and workers, the risks to these individuals are determined not to be of concern.

For bystanders, exposure is expected to be much less than that for workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Acetamiprid Is Introduced Into the Environment?

Acetamiprid poses a potential risk to non-target organisms including terrestrial plants, marine-estuarine invertebrates (such as the mysid shrimp) and honeybees. Therefore, risk-reduction measures including precautionary label statements and buffer zones must be observed.

The environmental fate and environmental toxicology of acetamiprid is described in REG2002-05.

The environmental transformation products of acetamiprid: IM-1-5 in soil, IM-1-4 in sediment, and IB-1-1 in water are not expected to accumulate or move in the environment, nor pose a risk to non-target organisms.

Acetamiprid will pose negligible risk to earthworms under conditions of field use. The risk to avian reproduction is also negligible. It will, however, pose a risk to aquatic invertebrates, non-target terrestrial plants and honey bees exposed to direct treatment. These risks can be mitigated by precautionary label statements and the establishment of terrestrial and aquatic buffer zones for protection of these habitats.

Value Considerations

What is the Value of Assail 70 WP Insecticide, Tristar 70 WSP Insecticide, Acetamiprid RTU Insecticide, and Vault 50 FS Insecticide Seed Treatment?

Pest control products containing acetamiprid control a variety of insect pests in various fruit, vegetable, ornamental, and oilseed crops.

Assail 70 WP Insecticide is registered for commercial use to control aphids, whitefly, Colorado potato beetle, tentiform leafminer, leafhoppers, codling moth, pear psylla, swede midge, oriental fruit moth, and pea leafminer on leafy vegetables, cole crops, certain fruiting vegetables, pome fruits, grapes, potato, and tobacco.

Tristar 70 WSP Insecticide is registered for commercial use to control European pine sawfly, aphids, tentiform leafminer, leafhoppers, and whiteflies on ornamentals, including trees, potted flowering plants, foliage plants, bedding plants, and flowers grown for cuttings, outdoors and in greenhouses, lathhouses, and shadehouses.

Acetamiprid RTU Insecticide is registered for domestic use to control aphids, European pine sawfly, leafhoppers, whiteflies, tentiform leafminer, and Colorado potato beetle on flowers and ornamental plants, leafy vegetables, cole crops, field tomatoes, and pome fruits.

Vault 50 FS Insecticide Seed Treatment is registered for commercial use as a seed treatment to control flea beetles on canola and mustard.

Please see the registered product labels for complete details of the registered uses.

Acetamiprid is an alternative to other insecticides currently registered for use on the pests and crops previously listed. Alternatives such as acetamiprid are needed to help prevent the development of resistance to registered insecticides and to provide replacements for older insecticides that may become unavailable as a result of re-evaluation.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of Acetamiprid Technical Insecticide, Assail 70 WP Insecticide, Tristar 70 WSP Insecticide, Acetamiprid RTU Insecticide, and Vault 50 FS Insecticide Seed Treatment to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

There is a concern for users coming into direct contact with acetamiprid on the skin or through inhalation of spray mists. Therefore, anyone mixing, loading or applying Assail 70 WP Insecticide must wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes. In addition, when mixing or loading certain amounts of product for application to potatoes they must also wear chemical-resistant coveralls and a respirator.

When mixing, loading or applying Tristar 70 WSP Insecticide for outdoor use, handlers and applicators must wear a long-sleeved shirt, long pants, socks and shoes, and chemical-resistant gloves. When applying indoors, handlers and applicators must wear chemical-resistant coveralls over a long-sleeved shirt and long pants, chemical-resistant gloves, rubber boots, goggles or faceshield, and a respirator.

For all tasks relating to treating seed (including mixing, loading, or treating) using Vault 50 FS Insecticide Seed Treatment, workers must wear chemical-resistant coveralls over long-sleeved shirt and long pants, chemical-resistant gloves, socks and shoes, and a respirator. Planters of treated seed must wear coveralls over long-sleeved shirt, long pants, socks and shoes, and chemical-resistant gloves.

A 12-hour restricted-entry interval (REI) for the agricultural products encompasses most postapplication tasks, however, it is necessary for longer REIs for some tasks on several crops, including cole crops, pome fruits and grapes. Other mitigation measures include the reduction of application rate, increased time interval between sprays and restrictions on the amount of product that can be handled in a day. Exposure concerns could not be reconciled for aerial use on potato crops; therefore, this use can not be supported. Standard label statements to protect against drift during application are on the label.

All use statements on the currently registered label of Acetamiprid RTU Insecticide are acceptable.

Environment

Key risk-reduction measures for the protection of the environment include precautionary label directions and buffer zones. These measures were originally described in REG2002-05 and are summarized here for the current end-use products and the technical active ingredient:

Assail 70 WP Insecticide and Tristar 70 WSP Insecticide

- Toxicity statements for aquatic organisms, non-target terrestrial plants, and bees
- Restriction of use when bees are in the area
- Terrestrial buffer zones of 2 m and 10 m for field sprayer and airblast application, respectively
- Aquatic buffer zones of 20 m and 30 m for field sprayer and airblast application, respectively

Vault 50 FS Insecticide Seed Treatment

- Toxicity statements for aquatic organisms, non-target terrestrial plants, bees and birds
- Directions to remove any seeds left on soil surface

Acetamiprid RTU Insecticide

- Toxicity statements for aquatic organisms, non-target terrestrial plants, and bees
- Restriction of use when bees are in the area
- No application to bodies of water and no application during gusty winds

Acetampirid Technical

- Toxicity statement for aquatic organisms, non-target terrestrial plants, and bees
- Precaution statement for discharge of effluent into bodies of water

Next Steps

Before making a final registration decision on acetamiprid, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

Other Information

When the PMRA makes its registration decision, it will publish a Registration Decision on acetamiprid (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

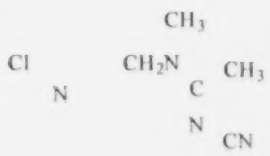
Acetamiprid

1.0 The Active Ingredient, Its Properties and Uses

A detailed assessment of the chemical properties and use information of acetamiprid, Assail 70 WP Insecticide, Acetamiprid RTU Insecticide and Tristar 70 WSP Insecticide are presented in Regulatory Note REG2002-05, *Acetamiprid, Assail Brand 70 WP Insecticide, Chipco Brand Tristar 70 WSP Insecticide, and Pristine Brand RTU Insecticide*.

The previously outstanding one year storage stability studies for the end-use products have been submitted to Health Canada's Pest Management Regulatory Agency (PMRA) and have been found to be satisfactory, with the exception of the storage stability study for Acetamiprid RTU Insecticide, which is still outstanding.

1.1 Identity of the Active Ingredient

Active substance	Acetamiprid
Function	Insecticide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	(*E*)-N^1-[(6-chloro-3-pyridyl)methyl]-N^2-cyano-N^1-methylacetamidine
2. Chemical Abstracts Service (CAS)	(1*E*)-*N*-[(6-chloro-3-pyridinyl)methyl]-*N'*-cyano-*N*-methylethanimidamide
CAS number	135410-20-7
Molecular formula	$C_{10}H_{11}ClN_4$
Molecular weight	222.68
Structural formula	

Active substance	Acetamiprid
Purity of the active ingredient	99.5% nominal

1.2 Physical and Chemical Properties of the Active Ingredients and End-use Product

Technical Product— Acetamiprid

Refer to REG2002-05 for a detailed summary of the physical and chemical properties of Acetamiprid.

End-Use Products—Assail 70 WP Insecticide and Acetamiprid RTU Insecticide

Refer to REG2002-05 for a detailed summary of the physical and chemical properties of Assail 70 WP Insecticide and Acetamiprid RTU Insecticide.

End-Use Product—Tristar 70 WSP Insecticide

Property	Result
Colour	Off-white (basic formulation) Light gray (alternate formulation)
Odour	Odourless
Physical state	Solid, fluffy
Formulation type	Wettable powder
Guarantee	70% nominal (limits: 67.9–72.1%)
Container material and description	Plastic and paper containers: 340 g, 480 g, 1.2 or 5 kg
Density	352.41 kg/m^3 (basic formulation) 251.49 kg/m^3 (alternate formulation)
pH of 1% dispersion in water	8.64 (basic formulation) 7.19 (alternate formulation)
Oxidizing or reducing action	No reaction was observed with tap water, hexane, monoammonium phosphate or zinc. Mild reaction with potassium permanganate.
Storage stability	The product is stable when stored for 24 months at ambient temperature in high density polyethylene containers.
Corrosion characteristics	Not corrosive
Explodability	Kst value = 96 bar·m/s This Kst value indicates capability for a weak explosion.

End-Use Product—Vault 50 FS Insecticide Seed Treatment

Property	Result
Colour	Blue
Odour	Smoky burnt sugar-like, sweet cookie-like odour.
Physical state	Liquid
Formulation type	Aqueous suspension
Guarantee	500 g/L nominal (limits: 485–515 g/L)
Container material and description	High-density polyethylene bottles or drums
Density	1.257 g/mL basic formulation 1.254 g/mL alternate formulation
pH of 1% dispersion in water	7.8
Oxidizing or reducing action	The product does not have any oxidizing properties as shown by lack of reaction with monoammonium phosphate, zinc or potassium permanganate.
Storage stability	The active concentration decreases slightly after one year storage at ambient temperature in the commercial container but remains within certified limits.
Corrosion characteristics	Not corrosive
Explodability	Not explosive

1.3 Directions for Use

Three end-use products are registered in Canada for foliar application by conventional ground equipment and an additional end-use product is registered for use as a seed treatment on canola and mustard. Consult the registered product labels for complete directions for use.

1.4 Mode of Action

Acetamiprid is an agonist of the nicotinic acetylcholine receptors in the synapses of the insect central nervous system. It is active on contact and through ingestion, with systemic and translaminar distribution in plants.

2.0 Methods of Analysis

Refer to REG2002-05 for a detailed assessment of the methods of analysis for acetamiprid, Assail 70 WP Insecticide, Acetamiprid RTU Insecticide and Tristar 70 WSP Insecticide.

2.1 Methods for Analysis of the Active Ingredient

The methods provided for the analysis of the active ingredient and the impurities in Acetamiprid Technical have been validated and assessed to be acceptable for the determinations.

2.2 Method for Formulation Analysis

The methods provided for the analysis of the active ingredient in the formulations have been validated and assessed to be acceptable for use as enforcement analytical methods.

2.3 Methods for Residue Analysis

The liquid chromatography with tandem mass spectrometry data gathering method submitted (method KP-216R1) as part of the confirmatory data package to convert the active ingredient, acetamiprid, from conditional registration to full registration was acceptable. The method fulfilled the requirements with regards to specificity, accuracy and precision at the limit of quantitation. Acceptable recoveries (70–120%) were obtained in matrices tested—grapes, tomatoes, cabbage and broccoli. Please refer to REG2002-05 for further information regarding the analytical methods for acetamiprid.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

Acetamiprid is a neonicotinoid insecticide that is structurally and functionally related to nicotine. It acts by binding or partially binding to specific areas of the nicotinic acetylcholine receptor. Normally, the neurostransmitter acetylcholine, which is released at neuronal and neuromuscular junctions in response to membrane depolarization, binds to the nicotinic acetylcholine receptor causing ion channels to open, leading to changes in ion flux and perpetuating the nerve impulse. When acetylcholine is subsequently destroyed by the enzyme acetylcholinesterase, the membrane returns to its normal resting state. However, binding of nicotinic acetylcholine agonists, such as neonicotinoids, to the nicotinic acetylcholine receptor leads to prolonged activation of the receptor, causing desensitization and blocking of the receptor. The result of such agonistic activity is excitation of the nervous system.

A detailed review of the toxicological database for the insecticide acetamiprid was conducted previously in 2002 and is summarized in REG2002-05. The 2002 review of the toxicological database revealed that acetamiprid did not elicit any specific target organ toxicity; generalized toxicity (in other words, decreases in body weight, body weight gain, food consumption and/or food efficiency) was observed as well as liver effects that were deemed to be indicative of a pharmacological effect rather than overt hepatotoxicity. There was no evidence of oncogenicity, genotoxicity or teratogenicity. There was qualitative evidence of increased susceptibility in offspring in the two-generation reproductive toxicity study. In that study, effects were noted in offspring and parental animals at the same dose level—800 ppm, the highest dose tested (HDT)—but the effects noted in the offspring (decreased litter size and viability and weaning

indices in F2 pups, delayed sexual maturation) were considered more serious than those that were observed in parental animals (reduced body weight, body weight gain, and food consumption). An additional threefold factor was applied to certain risk assessments in 2002 to account for this increased susceptibility. A developmental neurotoxicity (DNT) study was required as a condition of registration.

A DNT study was submitted to the PMRA and reviewed as part of the application to convert the registration status of acetamiprid from conditional to full registration. In addition to the DNT study, the applicant provided an acute oral toxicity study conducted with the soil metabolite IM-1-5 in corn oil, an additional acute oral toxicity study in which acetamiprid was administered in corn oil to rats, and a metabolism study in rats with the purpose of determining the excretion balance of IM-1-5. These acute and metabolism studies were not required to support the conversion from conditional to full registration.

The acute oral toxicity studies conducted with IM-1-5 and acetamiprid showed that the acute toxicity of IM-1-5 is similar to that of acetamiprid when administered in corn oil. Results from the metabolism study showed that IM-1-5 is a minor metabolite in the rat (4.5% and 0.4% of the administered dose in the urine of the low- and high-dose groups, respectively, with none detected in the feces).

In the DNT study, dosing of dams occurred from the sixth day of gestation to the end of the lactation period. One dam dosed with 45 mg/kg bw/day of acetamiprid, the highest dose tested, died during parturition on gestation day 23. Three dams from this dose group lost their entire litters prior to postnatal (PND) day 1 due to stillbirths and/or early pup deaths, resulting in [illegible] mean litter size and live birth and viability indices. Additional indications of maternal toxicity [illegible] dose in the form of increased incidences of several clinical signs as well as reduced body weight, body weight gain and food consumption during the gestation period. Effects noted in offspring of the dams dosed with 45 mg/kg bw/day included hair loss and decreased body weights during lactation and after weaning.

Behavioural testing of offspring revealed decreases in auditory startle responses in males from the 10 and 45 mg/kg bw/day dose groups on PND 20 and 60 and in females from the 45 mg/kg bw/day dose group on PND 20. However, there was no effect on startle habituation at any dose level. It is noteworthy that exposure to nicotine (which is structurally related to acetamiprid) during the neonatal period has been shown to result in auditory-cognitive deficits in adult rats, manifested as impaired performance on an auditory-cued active avoidance task (Liang et al. 2006).

High variability in the results from the motor activity and learning and memory testing confounded the interpretation of these results. However, an apparent treatment-related impairment in recall ability among males from the 45 mg/kg bw/day dose group (HDT) was noted in the assessment of learning and memory. The type of testing conducted for the assessment of learning and memory (Biel maze) is a fairly complex test when compared to other types of water maze or passive avoidance testing employed in DNT studies.

The morphometric assessment of offspring from the 45 mg/kg bw/day dose group (HDT) revealed possible treatment-related changes in certain brain measurements, including increased thickness of the pons in males on PND 11, decreased length of the ventral limb of the dentate gyrus in both males and females on PND 72, increased vertical thickness of the cortex in females on PND 11, and increased vertical height between the hippocampal pyramidal neuron layers in females on PND 11. A definitive no observed adverse effect level (NOAEL) for changes in brain morphometry could not be determined since these measurements were not conducted in offspring from the low- (2.5 mg/kg bw/day) and mid- (10 mg/kg bw/day) dose groups. In assessing the level of concern (LOC) for the missing brain morphometric data, the following was taken into consideration: (1) a NOAEL for behavioural assessments (for example, auditory startle) was established at the lowest dose tested, (2) the endpoint of auditory startle could be affected in the absence of brain morphometric changes, and (3) an 18-fold margin exists between the NOAEL for auditory startle (2.5 mg/kg bw/day) and the dose at which changes in brain morphometrics were noted (45 mg/kg bw/day). Therefore, the LOC over the lack of brain morphometric data from the low- and mid-dose groups is low.

The results from the DNT study provided additional information regarding increased susceptibility in the young qualitatively indicated previously in the reproductive toxicity study, as reduced auditory startle effects in male offspring exposed in utero were noted at doses that did not cause adverse effects in maternal animals. The NOAEL for offspring in the DNT study was 2.5 mg/kg bw/day, based on reduced auditory startle in males.

It should be noted that the reporting of the positive control data submitted with the DNT study was limited in terms of the information provided (data presentation was limited to graphs for most parameters, no individual data were provided and histopathological changes to the peripheral nervous system were not demonstrated). However, it did provide evidence that the conducting laboratory is able to elicit and detect changes in neurobehavioural endpoints.

Any limitations identified in the DNT study (variable motor activity data, lack of brain morphometric measurements at low and mid doses and limited positive control data) did not hinder the PMRA's ability to properly evaluate the results of the DNT study. Therefore, the DNT study was considered acceptable for regulatory purposes.

As a consequence of the submission and review of the required DNT study, a re-examination of the endpoints selected for dietary, occupational and residential exposure assessments was undertaken. Results of the newly submitted studies conducted on laboratory animals, as well as the toxicological endpoints selected for the human health risk assessment, are summarized in Appendix I, Tables 2, 3 and 4.

In assessing the occupational, residential and dietary risks from potential exposure to acetamiprid products, the standard uncertainty factor of 100-fold has been applied to account for interspecies extrapolation and intraspecies variability. Additional factors were applied to protect the population from relevant endpoints of concern as well as to accommodate *Pest Control Products Act* considerations.

3.1.1 *Pest Control Products Act* Hazard Characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to take into account completeness of the data with respect to the exposure of and toxicity to infants and children and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database for the assessment of risk to infants and children, the database contains the full complement of required studies including developmental toxicity studies in rats and rabbits, a reproductive toxicity study in rats and a DNT study in rats. While there were some limitations in the DNT study as noted, the study was considered acceptable for regulatory purposes.

With respect to identified concerns relevant to the assessment of risk to infants and children, sensitivity of the young was identified in the reproductive toxicity and DNT studies. In the reproductive toxicity study, effects noted in the offspring (in other words, decreased litter size and viability and weaning indices in F2 pups, delayed sexual maturation in F1 pups) were considered more serious than those that were observed in parental animals (in other words, reduced body weight, body weight gain, and food consumption) at the same dose level. In the DNT study, effects on auditory startle response were noted in male offspring at a dose that did not cause adverse effects in maternal animals.

As mentioned earlier, acetamiprid is a neonicotinoid that is structurally related to nicotine. Studies in the published literature suggest that exposure to cigarette smoke causes developmental toxicity, including functional deficits, in humans that are exposed prenatally (Slotkin, 2008). Maternal smoking during pregnancy has been identified as a risk factor for the development of attention deficit hyperactivity disorder in children (Banerjee et al. 2007).

Although nicotine is not the only constituent of cigarette smoke, there is ample evidence linking nicotine exposure to effects on the developing nervous system (Dwyer et al. 2008). The published literature contains numerous studies demonstrating neurotoxicity in developing animals exposed to nicotine in utero (Ajarem and Ahmad, 1998; Vaglenova et al. 2004; Thomas et al. 2000; Shacka et al. 1997; Levin et al. 1993). Effects noted in offspring following prenatal nicotine exposure in the aforementioned animal studies included delayed eye opening, delayed sensory motor reflexes, hyperactivity, increased anxiety, poor adaptation in a new environment, increased stereotypy and alterations in cognitive performance. One of these studies also demonstrated neurotoxic potential in male offspring only, which suggested that the central control of motor function in males is more sensitive to the effects of gestational nicotine exposure compared to that of females (Shacka et al. 1997).

In rats, prenatal nicotine exposure has been shown to cause cell death and a decline in the central nervous system cell number (Slotkin, 1998). The postulated mode of action for nicotine involves disruption of the processes of cell development and cell signaling, which results in alterations to the developing cholinergic, catecholaminergic and serotoninergic neurotransmitter systems. This mode of action is believed to be plausible in humans because the nicotine receptor is present in the developing human brain (Slikker et al. 2005).

These data should be considered when assessing the effects of acetamiprid on the developing young. The available bioassays conducted with acetamiprid were not designed to test for more subtle neurotoxic effects such as attention deficit disorders, mood disorders and depression. The neurobehavioural effects observed in the DNT study conducted with acetamiprid signal the potential for functional effects on the nervous system. While auditory startle response is known to represent a reflex involving sensory and muscular systems, there is a cognitive component as well. Thus, a treatment-related alteration in auditory startle response may manifest as a wide range of neurotoxicity in humans. It is not known how serious such effects may be in a developing hu nan.

In summary, all of the required studies relevant to assessing risk to infants and children were available and a NOAEL for a neurobehavioural endpoint, considered to be a sensitive indicator of neurotoxicity, was identified in the DNT study. Although there was increased sensitivity of the young demonstrated in the toxicological database, the endpoints selected for risk assessment, as outlined below, are based on the effect of concern (in other words, developmental effects in pups following prenatal, postnatal exposure, or both). As previously noted, however, there is some residual concern regarding the seriousness of the endpoint observed in the DNT study—in other words, the manner in which this endpoint would manifest in a developing human. On the strength of all the available information, therefore, the *Pest Control Products Act* factor was retained, but reduced to threefold.

3.2 Determination of Acute Reference Dose

The recommended acute reference dose (ARfD) for acetamiprid is 0.008 mg/kg bw. The most appropriate study for selection of a toxicity endpoint for acute dietary exposure was the DNT study, in which a NOAEL of 2.5 mg/kg bw/day was determined in male offspring based on reduced auditory startle response at the lowest observed adverse effect level of 10 mg/kg bw/day. The neurological effects noted in offspring in this study may occur following a single exposure; therefore, these effects are relevant to the selection of the ARfD. The NOAEL in the DNT study is the lowest NOAEL of the database, is protective of the most sensitive subpopulation, and provides a lower ARfD than established in 2002 (0.1 mg/kg bw). The previous ARfD was based on the NOAEL of 10 mg/kg bw from the acute neurotoxicity study in rats.

Uncertainty factors of 10-fold for interspecies extrapolation as well as 10-fold for intraspecies variability were applied in the setting of the ARfD. As indicated above, a threefold *Pest Control Products Act* factor was retained. This results in a Composite Assessment Factor (CAF) of 300.

The ARfD is calculated according to the following formula:

$$\text{ARfD} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{2.5 \text{ mg/kg bw}}{300} = 0.008 \text{ mg/kg bw of acetamiprid}$$

3.3 Determination of Acceptable Daily Intake

The recommended acceptable daily intake (ADI) for acetamiprid is 0.008 mg/kg bw/day. The most appropriate study for selection of a toxicity endpoint for chronic dietary exposure was the DNT study, in which a NOAEL of 2.5 mg/kg bw/day was determined in male offspring based on reduced auditory startle response at the lowest observed adverse effect level of 10 mg/kg bw/day. This is the lowest NOAEL of the database, is protective of the most sensitive subpopulation, and provides a lower ADI than established previously in 2002 (0.023 mg/kg bw/day). The previous ADI was based on the NOAEL of 7.1 mg/kg bw/day from the chronic toxicity and oncogenicity study in rats

Uncertainty factors of 10-fold for interspecies extrapolation as well as 10-fold for intraspecies variability were applied in the setting of the ADI. As indicated above, a threefold *Pest Control Products Act* factor was retained. This results in a CAF of 300.

The selected ADI provides margins in excess of 850 and 2100 to the NOAELs in the chronic and reproductive toxicity studies, respectively.

The ADI is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{2.5 \text{ mg/kg bw/day}}{300} = 0.008 \text{ mg/kg bw/day of acetamiprid}$$

3.4 Occupational and Residential Risk Assessment

3.4.1 Toxicological Endpoints

Occupational exposure to acetamiprid is characterized as short- to long-term duration and is predominantly by the dermal and inhalation routes.

For short-, intermediate- and long-term occupational exposures via the dermal and inhalation routes, the NOAEL of 2.5 mg/kg bw/day from the DNT study was selected. Offspring toxicity was observed in the DNT study in the form of reduced auditory startle in males. Worker populations could include pregnant or lactating women; therefore, this endpoint was considered appropriate for the occupational risk assessment. The available 21-day dermal study did not assess the relevant endpoints of concern (in other words, developmental effects in pups following prenatal and/or postnatal exposure).

The target margin of exposure (MOE) for these scenarios is 300, which includes uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability, as well as a threefold factor to account for the residual concern regarding the seriousness of the endpoint observed in the DNT study (in other words, the manner in which this endpoint would manifest in a developing human).

Aggregate risk assessment

Short-term aggregate exposure to acetamiprid may comprise food, drinking water and residential (dermal, inhalation and incidental oral) exposures. The most sensitive indicator of exposure to acetamiprid is reduced auditory startle in male offspring in the DNT study. Therefore, for the oral, dermal and inhalation components of exposure, the NOAEL of 2.5 mg/kg bw/day in male offspring from the DNT study in the rat was selected. The target MOE of 300 was chosen for all populations and exposure scenarios to account for interspecies extrapolation (10-fold) and intraspecies variability (10-fold), and includes a threefold factor to account for the residual concern regarding the seriousness of the endpoint observed in the DNT study—in other words, the manner in which this endpoint would manifest in a developing human. This MOE would be protective of other endpoints seen in the database.

3.4.1.1 Dermal Absorption

The PMRA reviewed a dermal absorption study submitted in support of the registration of the acetamiprid end-use products. The dermal absorption value of 30%, for regulatory purposes, was derived from the highest direct absorption of 6.34% with the addition of the skin-bound residue of approximately 25% at the 24-hour interval. As the dermal absorption values of other similar pesticides are lower than 30%, the PMRA considered a refined estimate for acetamiprid based on a weight-of-evidence approach.

Consideration was given to the oral-dermal toxicity, physical and chemical characteristics, and dermal absorption of acetamiprid compared to similar compounds. A comparison to clothianidin, another single-ringed neonicotinoid, is shown in Appendix I, Table 5.

The dermal absorption values derived from in vivo studies of other actives including neonicotinoids suggested that the absorbed dose during the exposure period was low, and thereafter, skin-bound residue is not very well absorbed.

Based on the low dermal absorption of skin-bound residue observed with other actives that include neonicotinoids with similar characteristics, and low dermal toxicity compared to oral toxicity, dermal absorption of skin-bound acetamiprid residue is likely to be low.

The dermal absorption of acetamiprid during a typical workday, based on the rat in vivo study, is best approximated by the 10-hour exposure of 4% of the applied dose. After a continuous exposure of 24 hours, the maximum dermal absorption was 6.3%. Given the similar characteristics to other neonicotinoids, a typical working day dermal exposure to acetamiprid would not be expected to significantly exceed 6.3%.

In order to be protective of human health, the PMRA, based on the weight-of-evidence, comparison of dermal absorption studies, oral and dermal toxicology, and physical-chemical properties, has determined that the available data support a 10% dermal absorption value for acetamiprid for regulatory purposes.

3.4.2 Occupational Exposure and Risk

3.4.2.1 Mixer/loader/applicator Exposure and Risk Assessment

Individuals have potential for exposure to acetamiprid during mixing, loading and application. Dermal and inhalation exposure estimates for workers mixing and loading wettable powder, water soluble packets and liquid suspension formulations, and wearing specified personal protective equipment, were generated from the Pesticide Handlers' Exposure Database version 1.1, from previously submitted study data, or from Outdoor Residential Exposure Task Force data.

The Pesticide Handlers Exposure Database data provided an adequate basis for estimating operator exposure for most of the proposed uses. The data were based on high confidence exposure database runs with similar personal protective equipment as proposed on the label and adequate numbers of replicates of A and B grade data. The Pesticide Handlers Exposure Database does not provide exposure estimates for clean-up/repair activities nor quantify the variability of exposure estimates.

Exposure to workers mixing, loading and applying acetamiprid is expected to be short- to long-term in duration and to occur primarily by the dermal and inhalation routes. Exposure estimates, shown in Appendix I, Tables 6, 7 and 8, were derived for mixers, loaders and applicators applying acetamiprid to: leafy and fruiting vegetables, cole crops, potatoes and tobacco using groundboom equipment; potatoes using aerial application; pome fruit using airblast equipment; outdoor and indoor (greenhouse, shadehouse and lathhouse) ornamentals using handheld equipment; and canola and mustard seed treatment in commercial facilities. The exposure estimates are based on mixers/loaders/applicators of Assail 70 WP Insecticide or Tristar 70 WSP outdoors wearing a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes. When applying Tristar 70 WSP Insecticide for indoor use, handlers and applicators must wear chemical-resistant coveralls, chemical-resistant gloves, rubber boots, goggles or faceshield, and a respirator. For all tasks when treating seed using Vault 50 FS Insecticide Seed Treatment, workers must wear chemical-resistant coveralls, chemical-resistant gloves and a respirator.

Chemical-specific data for assessing human exposures during pesticide handling activities were submitted. Studies were previously submitted and reviewed for exposure estimates of mixers, loaders and treaters and planting of treated seed.

Dermal exposure was estimated by coupling the unit exposure values with the amount of product handled per day and the dermal absorption factor. Inhalation exposure was estimated by coupling the unit exposure values with the amount of product handled per day with 100% inhalation absorption. Exposure was normalized to mg/kg bw/day by using 70 kg adult body weight.

Exposure estimates were compared to the toxicological endpoint (the NOAEL) of 2.5 mg/kg bw/day, to obtain the MOE; the target MOE is 300.

Most uses were considered acceptable with some uses requiring additional mitigation measures. The application rate for cole crops treated with Assail 70 WP Insecticide is reduced, to address unacceptable exposure for mixers and loaders, necessitating the removal of the whitefly pest. The aerial application to potato treated with Assail 70 WP Insecticide is considered unacceptable due to mixer and loader exposure concerns, necessitating the removal of aerial application for this crop. Only ground application is now supported.

3.4.2.2 Exposure and Risk Assessment for Workers Entering Treated Areas

There is potential for exposure to workers re-entering areas treated with acetamiprid products. Re-entry activities may include scouting, hand harvesting, irrigating, hand pruning, topping, tying, and thinning. Given the nature of activities performed, dermal contact with treated surfaces should not present an exposure concern when restricted entry intervals are observed. When sprays have dried, acetamiprid is not volatile, and therefore is not an inhalation concern.

The duration of exposure is considered to be of short- to intermediate-term duration for workers performing tasks for outdoor crops, and long-term duration for workers engaged in tasks for greenhouse, shadehouse or lathhouse crops. The primary route of exposure for workers re-entering treated areas would be through the dermal route.

Dermal exposures to workers entering treated areas are estimated by coupling dislodgeable foliar residue values with activity-specific transfer coefficients. Transfer coefficients are based on reviewed Agricultural Re-Entry Task Force studies and United States Environmental Protection Agency Policy 3.1 data. Chemical-specific dislodgeable foliar residue data were not submitted for acetamiprid. As such, a default dislodgeable foliar residue value of 20% of the application rate on the day of application was used in the exposure assessment. A daily residue dissipation of 10% was used for outdoor applications, and no dissipation for greenhouse, shadehouse, and lathhouse use. Exposure and risk assessments for the agricultural products are shown in Appendix I, Table 9 and Table 10. Exposure estimates were compared to the toxicological endpoint of 2.5 mg/kg bw/day to obtain the calculated MOE; the target MOE being 300.

For Tristar 70 WSP Insecticide, postapplication exposure was initially considered unacceptable for conducting tasks associated with flowers grown for cuttings. Mitigation is required by reducing the application rate for indoor use and, additionally, increasing the spray interval of outdoor applications. All postapplication entry was then acceptable for all crops with tasks for certain crops requiring restricted entry intervals as mitigation measures.

3.4.3 Residential Exposure and Risk Assessment

3.4.3.1 Handler Exposure and Risk

Individuals have potential for exposure to acetamiprid during application of Acetamiprid RTU Insecticide for outdoor domestic use. Dermal and inhalation exposure were estimated for adult homeowners using hand trigger or aerosol sprayers. Exposure and risk estimates are shown in Appendix I, Table 11.

Chemical-specific data for assessing human exposures during pesticide handling activities were not submitted for acetamiprid.

The Outdoor Residential Exposure Task Force data provided an adequate basis for estimating homeowner exposure. Exposure to homeowners applying acetamiprid is expected to be short-term in duration and to occur primarily by the dermal and inhalation routes. Exposure estimates were derived for homeowners applying Acetamiprid RTU Insecticide to flowering and ornamental plants, leafy vegetables, brassica crops, field tomatoes and ground cherries, and pome fruit listed on the label. The exposure estimates are based on homeowner applicators wearing a short-sleeved shirt, short pants and no gloves.

Dermal exposure was estimated by coupling the unit exposure values with the amount of product handled per day and the dermal absorption factor. Inhalation exposure was estimated by coupling the unit exposure values with the amount of product handled per day with 100% inhalation absorption. Exposure was normalized to mg/kg bw/day by using a body weight of 70 kg for an adult.

Exposure estimates were compared to the toxicological endpoint (NOAEL) of 2.5 mg/kg bw/day from the rat DNT study, to obtain the MOE. The MOE was well above the target MOE of 300 and, therefore, not of concern.

3.4.3.2 Postapplication Exposure and Risk

Postapplication exposure may occur during entry to treated residential areas. Residential outdoor ornamentals have a transfer co-efficient of 4000 cm^2/h. This value covers homeowner activities in residential outdoor ornamentals (flowers and shrubs only) and activities in residential gardens. Exposure and risk estimates are shown in Appendix I, Table 12.

The label for Acetamiprid RTU Insecticide states, "Keep children and pets out of treated areas until sprays have thoroughly dried". Exposure is expected from postapplication dermal contact with treated foliage for adults, youth, and children from residential use. Young children are not expected to spend significant time in a vegetable or flower garden, and therefore no significant exposure is expected for them. Since acetamiprid is not volatile and outdoor air levels are subject to infinite dilution, dermal exposure was considered adequate to address contact with treated areas and not of concern.

3.4.3.3 Bystander Exposure and Risk

Bystander exposure during mixing, loading, and application in a commercial operation is expected to be negligible because the potential for drift is expected to be minimal. Application is limited to agricultural crops only when there is low risk of drift to areas of human presence.

3.4.3.4 Aggregate Assessment

3.4.3.4.1 Residential Aggregate Assessment

A short-term residential aggregate assessment is presented as there is potential for the co-occurrence of spraying residential pome fruit trees, performing postapplication tasks related to treated fruit trees or vegetable garden crops, and dietary intake of acetamiprid.

Taking into account the number of applications and the spray intervals, there is possible contact with residues over an extended period (intermediate-term). Only an adult was considered to be the person applying the pesticide, and having dermal and inhalation exposure. Both adults and youth have exposure potential by conducting postapplication gardening (fruit, vegetables and ornamentals) activities and dietary intake (chronic-term). A child (1-6 year-olds, generally considered to be the most susceptible to toxic effects, based on a higher surface area to weight ratio) exposure was not quantified, since they would not be involved in spraying, and would not participate significantly in activities where crops have been treated (Appendix I, Table 13).

The residential aggregate exposure and risk estimates associated with the domestic use activities achieve acceptable MOEs for all at-risk subpopulations. Therefore, residential use and postapplication activities are acceptable when using Acetamiprid RTU Insecticide and following label directions.

3.4.3.4.2 Acute Pick-Your-Own Aggregate Assessment

An aggregate risk assessment is required as adults, youth and children have potential for exposure to acetamiprid residues from both oral (dietary food and drinking water) and dermal routes (pick-your-own or U-pick operations). The dermal exposure values calculated from picking treated apples (considered to be U-pick crops of apples and pears) were added to the single-day acute consumption of apples and to the chronic dietary exposure representing background levels in all foods and drinking water, to give a single-day estimate of exposure to members of the public who pick the fruit and eat it on the same day. Exposure and risk estimates are shown in Appendix I, Table 14.

The offspring NOAEL of 2.5 mg/kg bw/day from the rat DNT study was considered to be the most protective for exposure, given the acute (one-time) or short-term (occurring over several visits) scenario of the public to U-pick operations. The target MOE was 300. Inhalation exposure was considered to be negligible, due to the low volatility of acetamiprid and the outdoor dilution effect, and was not quantified.

The postapplication aggregate exposure and risk estimates associated with U-pick scenario activities achieve acceptable MOEs for all subpopulations. Therefore, the use of Assail 70 WP Insecticide in U-pick operations for apples and pears is acceptable.

3.5 Food Residues Exposure Assessment

3.5.1 Residues in Plant and Animal Foodstuffs

Confirmatory supervised residue trials conducted throughout Canada using end-use products containing acetamiprid confirmed the conclusions reached in the initial evaluation. Therefore, please refer to REG2002-05 for information pertaining to the residues in plant and animal foodstuffs.

3.5.2 Dietary Risk Assessment

Acute and chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.0), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals, 1994–1996 and 1998.

3.5.2.1 Chronic Dietary Exposure Results and Characterization

A basic chronic exposure analysis conducted using Canadian and American Maximum Residue Limits (MRLs) and default processing factors, indicated that the potential chronic exposure to acetamiprid for the general population was 76% of the ADI (food only). The exposure for the various subpopulations ranged from 51% to 307%, with the most exposed population being children aged one to two years. Following extensive refinements to the input data to include American and/or Canadian Supervised Trials Median Residue or complete field trial data sets, monitoring data for apples from the Pesticide Data Program, experimental processing factors, preliminary percent crop treated data from Canada, finalized percent crop treated data from the United States, and anticipated residues for milk and animal commodities where available, the exposure of the general population was reduced to 2.0% of the ADI (food only). Aggregate exposure from food and water (estimated environmental concentration (EEC) value = 3.16 µg a.i./L, Level II) was considered acceptable and below the LOC for all subpopulations, ranging from 2.1% to 8.4% of the ADI, with infants aged less than one year and children aged one to two years being the most exposed population subgroups.

3.5.2.2 Acute Dietary Exposure Results and Characterization

A basic acute exposure analysis, conducted using Canadian and American MRLs and default processing factors, indicated the potential acute exposure to acetamiprid for the general population was 247% of the ARfD, with the exposure for the various subpopulations ranging from 143% to 807% at the 95th percentile (food only; deterministic analysis). Following extensive refinements to the input data to include American and/or Canadian maximum residues or complete field trial data sets, monitoring data for apples (Pesticide Data Program), experimental processing factors, percent crop treated data from the United States and Canada,

and anticipated residues for milk and animal commodities, the probabilistic acute assessment indicated that exposure of the general population was reduced to 36.8% of the ARfD (food only; 99th percentile) with the exposure for the various subpopulations ranging from 28.8% to 88.5% at the 99th percentile. Aggregate exposure from food and water (Level II EEC value = 10.99 µg a.i./L) ranged from 32.2% to 95.0 % of the ARfD (99th percentile; probabilistic) for all population subgroups. The most exposed subpopulation was children aged one to two years.

Normally, in a highly refined probabilistic assessment, the acute risk is assessed at the 99.9th percentile since the majority of the input values would be obtained from monitoring data, which provides accurate data with respect to residues to which the population would be exposed. However, in this case, since the apple residue data were the only monitoring data used and the rest of the data were obtained from residue field trials, which provide a more conservative estimate of risk, it is acceptable to assess the risk of exposure to acetamiprid at the 99th percentile. Furthermore, a critical exposure contribution analysis report was conducted to determine the commodities that were driving the exposure to acetamiprid from food and water in children aged one to two years. The critical commodities (in other words, those contributing >5% of exposure) were determined to be collards (9.2%), grapefruit juice (8.5%), and apple juice (8.0%). Collards and grapefruit were conservatively evaluated using a single maximum value from field trials (in other words, probabilistic analysis was not conducted for collards and grapefruit).

3.5.3 Proposed Maximum Residue Limits

Table 3.5.1 Proposed Maximum Residue Limits

MRLs (ppm)	Foods
No MRLs are being recommended as a result of the conversion to full registration.	

For additional information on MRLs, refer to Health Canada's List of MRLs regulated under the *Pest Control Products Act*.

The nature of the residues in animal and plant matrices, analytical methodology, field trial data, and the acute and chronic dietary risk estimates are summarized in Appendix I, Tables 1, 15 and 16.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

The environmental fate of acetamiprid is described in REG2002-05.

Additional information/data submitted by the applicant in order to address the fate of the environmental transformation products IM-1-5 formed in the soil, IM-1-4 formed in the sediment, and IB-1-1 formed in the water indicated that these transformation products are not expected to accumulate nor become mobile in the environment. These transformation products are not expected to pose a risk to non-target organisms.

4.2 Effects on Non-Target Species

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. Estimated environmental exposure concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models that take into consideration application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (at the community, population, or individual level).

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC = 1). If the screening level RQ is below the LOC, the risk is considered negligible and no further risk characterization is necessary. If the screening level RQ is equal to or greater than the LOC, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

The estimated environmental concentrations of acetamiprid in soil, water, vegetation and other food sources for wild animals have been described in the initial review document REG2002-05.

The initial environmental toxicology review of acetamiprid identified the need for data on the toxicity to terrestrial organisms including earthworms, toxicity of foliar residues to honey bees, reproductive toxicity to wild birds (bobwhite quail and mallard duck) and toxicity to a plant species (lettuce). Data was also needed on toxicity to aquatic organisms including freshwater invertebrates (a midge and an amphipod species) and to early life stages of fish. A summary of the review of these data follows.

4.2.1 Effects on Terrestrial Organisms

Non-target Terrestrial Invertebrates
The 14-day LC_{50} to the earthworm, *Eisenia foetida*, is 9 mg a.i./kg soil. Given that the EEC of acetamiprid in soil is 0.19 mg a.i./kg, and the safety factor in the calculation is two, the resulting RQ value (0.04) indicates that the LOC is not exceeded for earthworms exposed to acetamiprid.

Acetamiprid belongs to the neonicotinoid class of insecticides, which are generally known to be highly toxic to bees. Data from the original review indicate that the acute contact LD_{50} is 8.09 µg a.i./bee and the acute oral LD_{50} is 14.5 µg a.i./bee. Additional information obtained from the scientific literature indicates bee toxicity values for acetamiprid are significantly higher (in other words, less toxic) than the majority of neonicotinoids. The acetamiprid transformation products are not a concern for toxicity to bees (Iwasa et al, 2004).

Data from the original review indicated that acetamiprid is moderately toxic to honey bees, *Apis mellifera*, exposed to direct oral and direct contact treatment under laboratory conditions. This triggered the need for an investigation of foliar application of acetamiprid under semi-field conditions. The results of studies conducted on 50 m^2 plots of flowering *Phacelia tanacetifolia* indicated that acetamiprid application had no adverse effect on the mortality of honey bees, flight activity of the bees on the crop, and behaviour of the bees in front of the hives and in the crop when applied at an application rate of 100 g a.i./ha in 400 L water/ha. No impact on condition of the colonies and brood development of honey bees was observed during the 27-day observation period. Thus, according to the submitted study data, the LOC is not exceeded under conditions of field use for honeybees exposed to acetamiprid.

Terrestrial Plants
The results of a multi-dose phytotoxicity study conducted with acetamiprid indicate that the EC_{25} for the most sensitive endpoint (shoot length) for vegetative vigour in lettuce, *Lactuca sativa*, is 6.5 g a.i./ha. Therefore, acetamiprid will pose a risk (RQ = 25.8) to the vegetative vigour in lettuce, if exposure occurs by overspray.

Wild birds
The most sensitive endpoint is adverse effects on reproduction of the mallard duck (*Anas platyrhynchos)* with a NOEC of 125 mg a.i./kg diet.

Wild birds, such as mallard duck, could potentially be exposed to acetamiprid residues as a result of spray drift or consumption of sprayed vegetation or contaminated prey. The mallard duck diet may consist of approximately 10% large insects or snails, 10% leafy plants and 80% grain. Since the EECs of acetamiprid on large insects, leaves/leafy plants and grain are 14.48, 527.78 and 14.48 mg a.i./kg dry weight, respectively, the estimated ingestion of acetamiprid through contaminated food sources by the mallard will be 65.81 mg a.i./kg dry weight.

The mallard duck (live weight 1.2 kg) consumes food equivalent to 4.17% of its body weight daily. Therefore, the bird would acquire a dose of 2.7 mg a.i./kg bw/day. This value is lower than the NOEC for the mallard duck (converted to 5.2 mg a.i./kg bw/day) at which there were no adverse reproductive effects on the test birds. Therefore, it is expected that the LOC for acetamiprid will not be exceeded on a reproductive basis for the mallard duck (RQ = 0.52).

4.2.2 Effects on Aquatic Organisms

Non-target Freshwater Invertebrates
The LC_{50} of acetamiprid to the midge, *Chironomus riparius*, and the amphipod, *Gammarus fasciatus*, are 24 µg a.i./L and 100 µg a.i./L, respectively. Given that the EEC of acetamiprid in water is 160 µg a.i./L, and the safety factor in the calculation is two, the LOC is exceeded for these aquatic invertebrates when exposed to acetamiprid (RQs = 13.3 and 3.2, respectively).

Fish Early-life Stages
Based on a NOEC of 19.2 mg a.i./L for the fathead minnow, *Pimephales promelas*, exposed to acetamiprid, and an EEC in water of 0.16 mg a.i./L, the resulting RQ value (0.008) indicates that the LOC for early-life stages of fish exposed to acetamiprid is not exceeded.

5.0 Value

A detailed assessment of the efficacy and value of Assail 70 WP Insecticide, Tristar 70 WSP Insecticide, and Acetamiprid RTU Insecticide is presented in REG2002-05. Since the initial registration, product names have been modified, four additional crops (potato, tobacco, ground cherry, and field pepper) and three additional pests (swede midge, Oriental fruit moth, and pea leafminer) have been added to the label of Assail 70 WP Insecticide, along with aerial application on potato in the prairie provinces, and an additional end-use product, Vault 50 FS Insecticide Seed Treatment, has been registered for use on canola and mustard seed.

5.1 Effectiveness Against Pests

To support full registration of acetamiprid and its associated end-use products, the applicant was required to submit additional efficacy data for control of aphids on leafy vegetables, cole crops, fruiting vegetables and pome fruits, whitefly on cole crops and fruiting vegetables, and tentiform leafminer and pear psylla on pome fruits with Assail 70 WP Insecticide; and for control of tentiform leafminer and European pine sawfly with Tristar 70 WSP Insecticide. Acceptable efficacy data were submitted for these uses and are reviewed in the following subsections.

5.1.1 Assail 70 WP Insecticide

Aphids on Leafy Vegetables, Cole Crops and Fruiting Vegetables

Efficacy data from the single trial submitted for leafy vegetables suggest that 39 g a.i./ha should be considered the lowest effective rate for control of aphids on leafy vegetables. Data from the two trials on cauliflower suggest that application rates as low as 14 g a.i./ha are statistically as effective as the highest tested application rate of 56 g a.i./ha, but also indicate that efficacy was inconsistent with an application rate of 39 g a.i./ha. Data from the two trials on tomato showed a weak trend towards increasing efficacy with increasing application rates, although levels of control were statistically similar at all application rates from 30 to 60 g a.i./ha. In the efficacy data submitted to support the original registration of this product, "applications at 56 g a.i./ha appeared to be consistently better than lower rates of 39–49 g a.i./ha" (REG2002-05), indicating that the higher rate may be justified as the lowest consistently effective rate. Considering all of these data, the currently registered application rates of 39–60 g a.i./ha for aphids on leafy vegetables, cole crops and fruiting vegetables can be supported with label directions to use the high rate under heavy pest pressure.

Aphids on Pome Fruits

Efficacy data from the five trials submitted for aphids on pome fruits indicate that results can be quite variable, but significant reductions in aphid infestations are most often achieved with application rates of 56 g a.i./ha or higher. Based on the efficacy data submitted in support of the original registration of this product, the proposed label claim for control of aphids on pome fruits was deemed acceptable "at the rate of 56–84 g a.i./ha, with the higher rate being recommended for control of high populations" (REG2002-05), but application rates lower than 56 g a.i./ha were not tested in those trials. The additional trials submitted in support of conversion to full registration indicate that application rates lower than 56 g a.i./ha are generally ineffective against aphids on pome fruits. In addition, higher application rates would be expected to be required in order to provide adequate coverage of the larger foliar volumes associated with tree fruits compared to field crops. Therefore, the currently registered application rates of 56–84 g a.i./ha for aphids on pome fruits can be supported with label directions to use the high rate under heavy pest pressure.

Whitefly on Cole Crops and Fruiting Vegetables

No additional efficacy data were submitted in support of conversion to full registration; however, the efficacy data submitted in support of the original registration of this product showed that the application rate of "84 g a.i./ha consistently provided better control than rates of 44–49 g a.i./ha" (REG2002-05). Although one study showed that the application rate of 56 g a.i./ha provided good control of whitefly, it was deemed inadequate on its own to establish 56 g a.i./ha as the lowest effective rate. Considering the small difference between 49 and 56 g a.i./ha, it is unlikely that 56 g a.i./ha would be consistently more effective than 49 g a.i./ha. Therefore, the currently registered application rate of 84 g a.i./ha for control of whitefly on cole crops and fruiting vegetables can be justified as the lowest consistently effective rate.

Tentiform Leafminer on Pome Fruits

Efficacy data from the two trials submitted for tentiform leafminer on pome fruits showed no statistical difference in efficacy among the three application rates tested (28–112 g a.i./ha) when the applications were made during egg hatch, but there was some indication of less numerical consistency of control at the lowest application rate compared to 56 g a.i./ha in the same trial (76% versus 85% reduction in percentage of mined clusters). Efficacy was clearly lower and less consistent when the application was made after egg hatch. Efficacy data submitted in support of the original registration of this product showed no improvement with application rates greater than 56 g a.i./ha, which was the lowest rate tested in those trials. Considering all of these data, the currently registered application rate of 56 g a.i./ha for tentiform leafminer on pome fruits can be supported. Label directions should be amended to specify targeting application for peak egg hatch of the first generation.

Pear Psylla on Pome Fruits

Efficacy data from the two trials submitted for pear psylla on pome fruits showed little evidence of any rate effect, with reductions in psyllid numbers ranging from 68 to 93% with application rates of 14–56 g a.i./ha and from 76 to 100% with application rates of 56–168 g a.i./ha, and no evidence of longer residual effects at higher application rates. Efficacy data submitted in support of the original registration of this product showed similar efficacy at all application rates tested (47–168 g a.i./ha) and some evidence that higher application rates (112 and 168 g a.i./ha) provided longer residual control. In one case "the 168 g a.i./ha rate appeared to perform better than the lower rates" but there was no apparent reason for the difference, in terms of pest pressure, and it was concluded that "additional data are needed to confirm the need and criteria for use of higher label rates (i.e., 168 g a.i./ha)" (REG2002-05). The efficacy data submitted in support of conversion to full registration do not confirm the need or criteria for use of the higher application rates. Therefore, application rates for pear psylla on pome fruits should be restricted to 56–112 g a.i./ha with label directions to use the high rate under heavy pest pressure.

5.1.2 Tristar 70 WSP Insecticide

The original registration of Tristar 70 WSP Insecticide for control of tentiform leafminer was based on efficacy data submitted to support the registration of Assail 70 WP Insecticide, which was granted temporary registration on the condition that additional efficacy data be submitted to demonstrate the lowest effective rate for various pests, including tentiform leafminer. Additional efficacy data for tentiform leafminer have been submitted to support the full registration of Assail 70 WP Insecticide and these data support the currently registered application rate of 56 g a.i./ha. Therefore, the currently registered application rate of Tristar 70 WSP Insecticide for control of tentiform leafminer (five packs or 56 g a.i./1000 L) can be supported.

Efficacy data from one trial were submitted in support of the original registration of Tristar 70 WSP Insecticide for control of European pine sawfly. In that trial, "substantial infestations" were reduced by 98–100% by 1 day after treatment with all application rates tested (28–112 g a.i./ha). Efficacy data from the two trials submitted in support of full registration show 100% control at even lower application rates. Therefore, there appears to be no justification for application rates of Tristar 70 WSP Insecticide greater than a single pack (11.2 g a.i.) per 1000 L to control European pine sawfly.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances [those that meet all four criteria outlined in the policy, in other words, persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*].

During the initial review process, acetamiprid and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, and evaluated against the Track 1 criteria. The results of that evaluation are described in REG2002-05. At that time, it was determined that acetamiprid and its major transformation products IM-1-2 and IC-0 do not meet all the TSMP criteria.

During the current review process, the PMRA has reached the conclusion that the transformation products IM-1-5 in soil, IM-1-4 in sediment and IB-1-1 in water also do not meet all the TSMP criteria, and therefore are not considered Track 1 substances.

6.2 Formulants and Contaminants of Health or Environmental Concern

Technical grade acetamiprid and the associated end-use products named in this document do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette*.

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for acetamiprid is adequate to define the majority of toxic effects that may result from human exposure to acetamiprid. In subchronic and chronic studies conducted with laboratory animals, generalized toxicity was manifested as effects on body weight and food consumption. In addition, mild, non-adverse liver effects resulting from an increased metabolic demand with increased exposure to acetamiprid were observed. Acetamiprid

was neither oncogenic nor genotoxic. There was qualitative evidence of increased susceptibility of the young in the reproductive toxicity study, in which the effects observed in offspring were more serious than those noted in parental animals. There was also evidence of increased susceptibility of the young in the DNT study, in which signs of potential neurotoxicity (reduced auditory startle response) were observed in male offspring at doses lower than those that caused effects in parental animals.

Exposure and risk assessments for the conversion of the four acetamiprid end-use products to full registration have been conducted, based on revised occupational toxicology endpoint and Uncertainty/Safety Factor selection, a revised dermal absorption value, and use scenario refinements. All currently registered end-use product uses are acceptable with mitigation measures.

Mixers, loaders and applicators handling acetamiprid and workers re-entering treated areas of crop fields, orchards, vineyards, outdoor ornamental nurseries, greenhouses, shadehouses and lathhouses, and residential gardens are not expected to be exposed to levels of acetamiprid that will result in an unacceptable risk when Assail 70 WP Insecticide, Tristar 70 WSP Insecticide and Vault 50 FS Insecticide Seed Treatment are used according to label directions. The personal protective equipment on the agricultural product labels is adequate to protect workers when mixing, loading, applying, and during clean-up and repair.

Residential exposure to individuals handling and contacting treated areas is not expected to result in unacceptable risk when Acetamiprid RTU Insecticide is used according to label directions.

The nature of the residue in plants and animals is adequately understood. Please refer to REG2002-05 for information pertaining to the residue definition and the proposed uses of acetamiprid. The proposed use of acetamiprid on various crops does not constitute an unacceptable chronic or acute dietary risk (through food and drinking water) to any segment of the population, including infants, children, adults and seniors. Sufficient crop residue data have been reviewed to recommend MRLs to protect human health. Please refer to Health Canada's List of MRLs regulated under the *Pest Control Products Act* for information pertaining to the MRLs for acetamiprid.

7.2 Environmental Risk

The environmental risk posed by acetamiprid is described in REG2002-05.

The additional information and data reviewed in this document indicate that acetamiprid will pose a risk to aquatic invertebrates and a dicotyledonous plant species. These risks can be mitigated by buffer zones and precautionary statements stipulated on the product label.

7.3 Value

All of the conditionally registered uses are considered acceptable for full registration, with adjustments to the application rates for pear psylla on pome fruits and for European pine sawfly.

7.4 Unsupported Uses

Use of Assail 70 WP Insecticide for control of whitefly on cole crops was deemed to pose a risk of unacceptable exposure to agricultural workers, thus, that use was removed from the label. As well, the aerial application to potato treated with Assail 70 WP Insecticide is considered unacceptable due to mixer and loader exposure concerns. Thus it is necessary to remove aerial application uses, with only ground application now being supported.

Use of Tristar 70 WSP Insecticide for indoor control of whitefly on flowers grown for cuttings was deemed to pose a risk of unacceptable exposure to workers. Thus, the use was removed from the label.

8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Acetamiprid Technical Insecticide, Assail 70 WP Insecticide, Tristar 70 WSP Insecticide, Acetamiprid RTU Insecticide and Vault 50 FS Insecticide Seed Treatment containing the technical grade active ingredient acetamiprid to control a variety of insect pests in various fruit, vegetable, ornamental, and oilseed crops.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

List of Abbreviations

µg	micrograms
a.i.	active ingredient
ADI	acceptable daily intake
ARfD	acute reference dose
ATPD	area-treated-per-day
bw	body weight
CAF	composite assessment factor
CAS	Chemical Abstracts Service
CEPA	Canadian Environmental Protection Act
cm	centimetre
d	day(s)
DAT	days after treatment
DNT	developmental neurotoxicity
EC_{25}	effective concentration on 25% of the population
EEC	estimated environmental concentration
et al	and others
F	female
F1	first filial generation
F2	second filial generation
FDA	*Foods and Drugs Act*
g	gram
h	hour(s)
ha	hectare
HAFT	highest average field trial
HDT	highest dose tested
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_{ow}	*n*-octanol– water partition coefficient
Kst	the product of the maximum rate of pressure rise and the third root of the special volume
L	litre
LOC	level of concern
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOAEL	lowest observed adverse effect level
LOQ	limit of quantitation
M	male
m^2	square metres
m^3	cubic metres
mg	milligram
mL	millilitre
M/L/A	mixer, loader, applicator
MOE	margin of exposure
MRL	maximum residue limit

MS	mass spectrometry
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
PHI	preharvest interval
PMRA	Pest Management Regulatory Agency
PND	postnatal day
ppm	parts per million
REI	restricted entry interval
RQ	risk quotient
TGAI	technical grade active ingredient
TSMP	Toxic Substances Management Policy

Appendix I Tables and Figures

Table 1 Residue Analysis

Matrix	Method ID	Analyte	Method Type	LOQ[a]		Reference
Plant	KP-216R1	acetamiprid	LC-MS/MS (data gathering)	0.01 ppm	grapes, tomatoes, cabbage and broccoli	1117904 1117905 1117906

Note: For all other methods please refer to REG2002-05
a. LOQ = limit of quantification

Table 2 Acute Toxicity of Acetamiprid Technical (NI-25) and One of its Metabolites (IM-1-5)

Study Type	Species	Result	Comment	Reference
Acute Toxicity of Acetamiprid Technical				
Oral (in corn oil)	Rat	LD_{50} = 195 mg/kg bw in M LD_{50} = 140–200 mg/kg bw in F	HIGH TOXICITY	1117947
Acute Toxicity of Metabolites of Acetamiprid				
Oral IM-1-5 (in corn oil)	Rat	LD_{50} = 141 mg/kg bw in M LD_{50} = 132 mg/kg bw in F	HIGH TOXICITY	1117946

Table 3 Toxicity Profile of Technical Acetamiprid

Study Type	Species	Results[a] (mg/kg/day)	Reference
Developmental Neurotoxicity	Rat	**Maternal NOAEL:** 10 mg/kg bw/day. **Maternal LOAEL:** 45 mg/kg bw/day, based on one mortality during parturition, increased incidence of clinical signs of toxicity during the dosing period (hair loss, scabbing, dried red material on forelimbs and around nose, decreased defecation), and reduced body weight, body weight gain and food consumption during gestation. **Developmental NOAEL (M):** 2.5 mg/kg bw/day. **Developmental NOAEL (F):** 10 mg/kg bw/day. **Developmental LOAEL (M):** 10 mg/kg bw/day, based on reduced auditory startle response. Effects noted at the next highest dose included reduced viability, hair loss, reduced body weight, and change in brain morphometry measurements. **Developmental LOAEL (F):** 45 mg/kg bw/day, based on reduced viability, hair loss, reduced body weight, decreased auditory startle response, and change in brain morphometry measurements. **Evidence of sensitivity of the young:** (effects were noted in the offspring at lower doses than in the maternal animals).	1117940
Metabolism - determination of IM-I-5 in excreta	Rat	IM-1-5 (soil metabolite) accounted for 4.5% and 0.4% of the administered dose in the urine of the low and high dose groups, respectively, and was not detected in the feces.	1117948

a. Effects observed in males as well as females unless otherwise reported

Table 4 Toxicology Endpoints for Use in Health Risk Assessment for Acetamiprid

Exposure Scenario	Dose (mg/kg bw/day)	Study	Endpoint	CAF[1] or Target MOE[2]	Reference
Acute Dietary	NOAEL = 2.5	Developmental Neurotoxicity	Reduced auditory startle response in male offspring.	300	1117940
	ARfD = 0.008 mg/kg bw				
Chronic Dietary	NOAEL = 2.5	Developmental Neurotoxicity	Reduced auditory startle response in male offspring.	300	1117940
	ADI = 0.008 mg/kg bw/day				
Short-, intermediate- and long-term dermal & inhalation	NOAEL = 2.5	Developmental Neurotoxicity	Reduced auditory startle response in male offspring.	300	1117940

[1] CAF = Composite Assessment Factor; relevant to dietary scenarios
[2] MOE = Margin of Exposure; relevant to occupational and bystander exposure scenarios

Table 5 Summary of Physical-chemical Characteristics of Acetamiprid Compared to Clothianidin

Compound (animal tested)	Exposure duration (h)	Mean direct absorption (% of applied dose)	Skin-bound residue (% of applied dose)	Dermal absorption value (% of applied dose)	Log K_{ow} (at 25°C)	Water solubility (g/L)	Molecular Mass (g/mole)	Structure
Acetamiprid (rat)	10 24	4.07 at 10h 6.34 at 24h	30.6 25.1	30	0.80	2.95 at 25°C	222.68	One-ring
Clothianidin (monkey)	8	0.24 at 120h	monkeys were not sacrificed; 96.99 – 98.46% dose recovery	1	0.7	0.327 at 20°C	250	One-ring

Table 6 Mixer and Loader Dermal and Inhalation Exposure Estimates for Assail 70 WP Insecticide

Scenario			Mixer/Loader				Applicator				Total Body Exposure	
Farmers and Custom applicators, unless otherwise stated	Crop	Application rate (kg a.i./ha)	Total Dermal unit exposure [a] (mg /kg a.i. handled)	Inhalation unit exposure [a] (mg /kg a.i. handled)	ATPD [b] (ha/day)	Body exposure [c] (mg a.i./kg bw/day)	Applicator Scenario Equipment	Total Dermal unit exposure [a] (mg /kg a.i. handled)	Inhalation unit exposure [a] (mg/kg a.i. handled)	Body exposure [c] (mg a.i./kg bw/day)	(inhalation + dermal) [d] (mg a.i./kg bw/day)	MOE (target =300)[e]
M/L/A	Cole crops	0.084	0.53138	0.0562	80	1.05×10^{-2}	Open cab, groundboom, Single layer + gloves	0.03249	0.00096	4.041×10^{-4}	1.090×10^{-2}	**229**
M/L/A	Leafy Vegetable, Cole crops; Fruiting vegetable (cherry tomato, peppers) Tobacco [f]	0.0602	0.53138	0.0562	80	7.522×10^{-3}		0.03249	0.00096	2.896×10^{-4}	7.812×10^{-3}	320
M/L/A	Fruiting Vegetables (field tomato)	0.084	0.53138	0.0562	32	4.199×10^{-3}		0.03249	0.00096	1.616×10^{-4}	4.360×10^{-3}	573
M/L/A farmer	Potato	0.0602	0.53138	0.0562	80	7.522×10^{-3}		0.03249	0.00096	4.041×10^{-4}	7.812×10^{-3}	320
M/L/A custom	Potato	0.0602	0.53138	0.0562	300	2.821×10^{-2}		0.03249	0.00096	1.086×10^{-3}	2.930×10^{-2}	**85**
M/L/A custom	Potato	0.0602	0.3391	0.00562 (with respirator)	13.33kg a.i./d; or approx 221.5 ha/d	7.753×10^{-3}		0.03249	0.00096	8.018×10^{-4}	8.332×10^{-3}	300
M/L for aerial[g]	Potato	0.0602	0.37114	0.0562	490	3.932×10^{-2}	Not applicable	——	——	——	3.932×10^{-2}	**64**

A for aerial	Potato	0.0602	——	——	490	——	Aerial (fixed- or rotary-winged aircraft)	0.01073	0.00007	4.817×10^{-4}	4.817×10^{-4}	5190
M/L/A	Pome fruit	0.168	0.53138	0.0562	16	4.199×10^{-3}	Open cab, airblast	0.56172	0.0058	2.380×10^{-3}	6.578×10^{-3}	380
M/L/A	Grapes	0.056	0.53138	0.0562	16	1.4×10^{-3}	Open cab, airblast	0.56172	0.0058	7.932×10^{-4}	2.193×10^{-3}	1140

Note: MOEs in **bold** do not achieve target. See row below for required mitigation, if appropriate.
M/L/A = mixer, loader and/or applicator;
a. All M/L/A wear single layer + gloves; in addition, M/L must wear respirator;
b. Default area treated per day (ATPD), PMRA database, using custom applicator ATPD, which also is considered to account for farmer use;
c. Total body Exposure = [application rate × ((dermal unit exposure × dermal absorption) + inhalation unit exposure) × ATPD × exposure duration] ÷ body weight ; dermal absorption value of 10%; body weight of adult = 70kg; youth = 39kg;
d. Total body exposure = M/L Exposure + Applicator Exposure;
e. Margin of exposure (MOE) = NOAEL ÷ Total Exposure; target = 300;
f. 95th percentile for tobacco farm size is 45ha; max. ATPD by farmer 25.6 ha (2006 Statistics Canada census);
g. Aerial application of product cannot be supported.

Table 7 Mixer, Loader and Applicator Exposure and Risk Assessments for Tristar 70 WSP Insecticide Containing Acetamiprid

Scenario			Mixer/Loader				Applicator				Total Body Exposure	
Farmers or Custom applicators	**Crop**	**Application rate (kg a.i./ha)**	**Total Dermal unit exposure [a] (mg/kg a.i. handled)**	**Inhalation unit exposure [a] (mg/kg a.i. handled)**	**ATPD [b] (ha/day)**	**Body exposure [c] (mg a.i./kg bw/day)**	**Applicator Scenario Equipment**	**Total Dermal unit exposure [a] (mg/kg a.i. handled)**	**Inhalation unit exposure [a] (mg/kg a.i. handled)**	**Body exposure [c] (mg a.i./kg bw/day)**	**(inhalation + dermal) [d] (mg a.i./kg bw/day)**	**MOE (target =300)[e]**
Outdoor use												
M/L/A [g] (WSP) [b]	Ornamentals (flowers for cuttings, bedding, foliage, potted)	0.112	1.974	0.1423	0.15	8.1528×10^{-5}	low-pressure handwand	——	——	——	8.153×10^{-5}	30700
M/L/A [f] (WSP)	Ornamentals (non-bearing fruit and nut trees, nurseries (including flowers))	0.112	0.02161	0.00018	3.75	1.4046×10^{-5}	High-pressure handwand	5.6071	0.151	4.257×10^{-3}	4.271×10^{-3}	585
M/L/A (WSP)	Ornamentals (non-bearing fruit and nut trees, nurseries (including flowers))	0.112	0.02161	0.00018	38	1.4233×10^{-4}	Open cab, groundboom	0.03249	0.0058	5.502×10^{-4}	6.925×10^{-4}	3610
M/L/A (WSP)	Ornamentals (non-bearing fruit and nut trees)	0.112	0.02161	0.00018	16	5.99296×10^{-5}	Open cab, airblast	0.56172	0.0058	1.587×10^{-3}	1.646×10^{-3}	1520

Indoor use												
M/L/A [a] (WSP) [h]	Ornamentals (flowers for cuttings, bedding, foliage, potted)	0.112	0.9932	0.1423	0.15	5.7989×10^{-5}	low-pressure handwand	—	—	—	5.799×10^{-5}	43100
M/L/A [c] (WSP)	Ornamentals (non-bearing fruit and nut trees, nurseries (including flowers))	0.112	0.02161	0.00018	3.75	1.4046×10^{-5}	High-pressure handwand	1.8271	0.0151	1.187×10^{-5}	1.201×10^{-5}	2080
M/L [i] (WSP)	Ornamentals (flowers for cuttings, bedding, foliage, potted)	0.112	0.02161	0.00018	7.2	2.6968×10^{-5}	Greenhouse, overhead sprinkler	—	—	—	—	92700

a. Assail 70WP: all M/L/A wear single layer + gloves; in addition, M/L must wear respirator. Tristar 70WSP: all M/L/A wear chemical-resistant coveralls over single layer + gloves and applicators must wear a respirator;

b. Area treated per day, using PMRA ATPD database, unless otherwise stated;

c. Total body exposure = [application rate × ((dermal unit exposure × dermal absorption) + inhalation unit exposure) × ATPD × Exposure duration] ÷ bw; dermal absorption value of 10%, bw of adult = 70kg, youth bw = 39kg;

d. Total body exposure = M/L exposure + applicator exposure;

e. MOE = NOAEL ÷ total exposure; target = 300;

f. 95th percentile for tobacco farm size is 45 ha; maximum ATPD by farmer 25.6 ha (2006 Statistics Canada census);

g. Used wettable powder + open pour/low pressure handwand scenario, combined mixer/loader/applicator, with 90% protection due to water soluble packets;

h. WSP = water soluble packaging formulation;

I. No data available for wettable powder with high pressure wand. Used M/L exposure for WSP formulation plus applicator of liquid / open pour / high pressure handwand scenario with no additional protection factor for the WSP formulation;

j. Mixer/loader only for automated application equipment (overhead sprinkler) for the maximum greenhouse area of 7.2ha (PMRA occupational database).

Table 8 Handling Exposure and Risk Estimates for Canola and Mustard Seed Treatment Using Vault 50FS Insecticide Seed Treatment

Task	Scenario Mitigation[a]	Application rate (kg a.i./kg seed)	Total dermal exposure units (mg a.i./kg a.i. handled)	Inhalation exposure units (mg a.i./kg a.i. handled)	Seed treated per day (kg seed/day)	Total body exposure (mg/kg bw/day)	Total MOE[b] target = 300
Mixer/Loader			0.0473	0.0117		0.003371	742
Other tasks	Commercial seed-treating facility: chemical-resistant coveralls + gloves; + respirator (representing a closed mix/load system)	0.0025 or 0.005	0.1295	0.0159	16000 at 0.0025 kg a.i./kg seed or 8000 at 0.005 kg a.i./kg seed	0.008309	301
All tasks			0.1165	0.0152		0.007526	332

a. 90% protection factor applied to dermal exposure (excluding head and hands) for chemical-resistant coveralls; 90% protection applied for gloves.

b. Total amount of active used per day = (application rate × amount of seed treated × 1000 g a.i./kg a.i.) ÷ 500 g a.i./L product = 80 L of product/day.

Table 9 Post-application Exposure and Risk Estimates for Agricultural End-use Products Containing Acetamiprid

Crop	Maximum application rate [a] (g a.i. /ha)	Number of applications	Post-application tasks	Exposure [b] (mg/kg bw/day)	MOE [c] (target = 300)	
					Range of tasks	Additional REI (days)
ASSAIL 70WP						
Leafy vegetables	60.2	5	Hand harvesting, thinning, pruning	0.0064	389	0
			Scouting	0.0039	648	
			Hand weeding, and tasks for minimal foliage	0.0013	1944	
Fruiting vegetables	84	2 field tomato	Hand harvest, staking, thinning training, tying	0.0035	717	0
			Irrigation, scouting, and staking/tying min. foliage	0.0024	1024	
			Irrigation, scouting, hand weeding min. foliage	0.0017	1434	
	60.2	4 ground cherry, peppers	Hand harvest, staking, thinning training, tying	0.0025	1000	0
			Irrigation, scouting, and staking/tying min. foliage	0.0017	1429	
			Irrigation, scouting, hand weeding min. foliage	0.0012	2000	
Tobacco	60.2	2	Hand harvest, Hand pruning, Stripping, thinning, topping, hand weeding	0.0041	615	0
			Irrigation, scouting	0.0026	945	
			Min. foliage scouting, thinning, hand weeding	0.0002	12290	
Potato	60.2	2	Irrigation, scouting full foliage	0.0031	819	0
			Irrigation, scouting min. foliage	0.0006	4097	
			Mechanical weeding, mechanical harvesting	No co-efficient	------	
Cole crops	60.2	5	hand harvest, irrigation, hand pruning, topping, tying mature plants, thinning	0.0129	194	4 (MOE=296, but using upper end TC, therefore acceptable)
			scouting mature plants	0.0103	243	2 (MOE=300)

Grapes	56	2	cane turning/girdling	0.0304	82	13 (MOE=324
			pruning, training, tying, thinning, leaf pulling	0.0134	187	5 (MOE=317)
			handline irrigation	0.0017	1445	0
			scouting, other minor contact tasks, or minimal foliage	0.0011	2271	0
Pome fruit	168	4	(hand) thinning	0.016	157	6 (MOE=295, but using upper end TC, therefore acceptable)
Apple U-pick			hand harvest, handline irrigation hand pruning, scouting hand harvest Adult Youth Child (1-6 yr) hand harvest			
			hand harvest	0.008	313	0
			handline irrigation	0.0058	940	0
			hand pruning, scouting	0.0027	427	0
			hand harvest (pick-your-own) Adult Youth Child (1-6 yr)	0.0010 0.0012 0.0019	2621 2121 1319	0
Tristar Brand 70WSP Insecticide						
Cut flowers (greenhouse, shadehouse, lathhouse)	34 or, 56	21	All tasks	0.0062 0.0051	402 488	0
Cut flowers (outdoors)	56	5	All tasks	0.0083	302	0
Potted plants, foliage plants, bedding plants, (greenhouse, shadehouse, lathhouse)	112	2	All tasks	0.002	1221	0
Potted plants, foliage plants, bedding plants, (outdoors)	112	5	All tasks	0.0017	1509	0

Ornamental trees, non-bearing fruit and nut trees (outdoors)	**112**	**5**	**Handline irrigation** **Scouting orchard crops**	**0.0046** **0.0021**	**549** **1207**	**0** **0**
Vault 50FS Insecticide Seed Treatment						
No postapplication, postplanting exposure is expected as seeds will be covered by soil.						

a. Assumed 20% dislodgeable foliar residue on the day of application; 10% daily dissipation for outdoor uses; 0% daily dissipation for greenhouse, shadehouse, and lathhouse use

b. $\frac{\text{DFR Value } (\mu g/cm^2) \times \text{Transfer Coefficient } (cm^2/h) \times \text{Hours Worked per Day (h)} \times \text{Conversion Factor } (1mg/1000\mu g) \times DA}{\text{Body Weight}}$

$$DFR = \text{Application rate } (\mu g/cm^2) \times \text{available residue fraction} \times \sum_{1}^{n} [\,(1\text{-dissipation rate})^{\text{postapplication day}}\,]$$

$\sum_{1}^{n}$ = summation of residue for each application

c. MOE = NOAEL/Exposure (target MOE = 300), according to SPN2003-04

Table 10 Post-Application (Planting) Exposure Estimate and Risk Assessments for Acetamiprid End-use Product Vault 50FS Insecticide Seed Treatment

Applicator scenario	Label max. application rates (kg a.i./kg seed)	Seeding rate per hectare (kg/ha)	Number of hectares sown per day (ha/d)	Total dermal exposure (mg a.i./kg a.i. handled)	Inhalation exposure (mg a.i./kg a.i. handled)	Total body exposure (mg a.i./kg bw/d)	MOE (target = 300) All tasks	Recommendations
Single layer, with gloves	0.005	9	100	1.845	0.248	0.00278	**90**	Mitigation measures required
Coveralls + gloves + respirator	0.0025	6	100	1.682	0.0248	0.00414	604	Max amount of a.i. handled per day is 3.02 kg a.i./day No REI once seed is planted
		9	100	1.682	0.0248	0.00827	302	
	0.005	6	100	1.682	0.0248	0.0062	403	
		9	100	1.682	0.0248	0.0124	**201**	
		9	67	1.682	0.0248	0.00831	301	

Note 1. Amount of canola seed planted: 3 kg a.i./d (typical); 4.5 kg a.i./d (maximum)
Note 2. Lower seeding rate of 6kg seed/ha; max. seeding rate of 9kg seed/ha (Canadian Canola Council); default hectares sown is 100 ha/d.
Note 3. Inhalation is a contributor to exposure, but would primarily occur during tasks directly related to seed (emptying seed bags into hopper, checking or bulk loading hopper), and therefore respirator not required for driving equipment.
Note 4. MOEs in **bold** do not achieve target. See row below for required mitigation.

Therefore, maximum amount of seed sown per day = (MOE/NOAEL) × BW /((TDE * DA) + IE)

Where, MOE = Margin of Exposure = 300
NOAEL = 2.5 mg/kg bw/day
BW = adult body weight of 70kg
TDE = Total Dermal Exposure (mg/kg bw/day)
DA = Dermal Absorption value = 10% = 0.1
IE = Inhalation exposure (assuming 100% systemic absorption) (mg/kg bw/day)

Table 11 Residential Handler Exposure and Risk Estimates from Using the Domestic End-use Product Acetamiprid RTU Insecticide

Scenario			Applicator			
Applicator scenario	**Crop**	**Amount of active handled per day [a,b] (kg a.i./day)**	**Dermal unit exposure [c] (mg a.i./kg a.i. handled)**	**Inhalation unit exposure [c] (mg a.i./kg a.i. handled)**	**Total body exposure [d] (dermal + inhalation) (mg a.i./kg bw/day)**	**MOE (target = 300) [d]**
Trigger sprayer, short-sleeved shirt and shorts, no gloves	Leafy vegetables, cole crops, fruiting vegetables, pome fruit, outdoor ornamental plants and trees	6.4×10^{-5} kg a.i./1 L container	130.123	0.0784	$1.19 \times 10^{-5} + 0.071 \times 10^{-6} = 1.197 \times 10^{-5}$	208 000

a. Surrogate study using trigger spray RTU and aerosol RTU sprayer (Outdoor Residential Exposure Task Force);
b. Equivalent use of one 1L container;
c. Total body exposure = [application rate × ((dermal unit exposure × dermal absorption factor) + inhalation unit exposure) × ATPD × exposure duration] ÷ body weight; dermal absorption value of 10%; bw = adult 70kg, youth 39kg;
d. Margin of exposure (MOE) = NOAEL ÷ total exposure; target = 300, where the NOAEL = 2.5 mg/kg bw/day.

Table 12 Post-application Exposure and Risk Estimates for the Domestic End-use Product Acetamiprid RTU Insecticide

Crop	Number of applications [a]	Application interval (days)	Highest postapplication transfer co-efficient [b] (cm^2/h)	Exposure [c] (mg/kg bw/day)	MOE (target = 300)	REI (days)
Adult bw = 70 kg						
Pome fruit	4	12	3000	0.0008	3062	0
Flowers, shrubs, leafy and cole vegetables	5	7	4000	0.0015	1701	
Youth bw = 39 kg						
Pome fruit	4	12	2066	0.001	2477	0
Flowers, shrubs, leafy and cole vegetables	5	7	2755	0.0018	1376	

Note: All preharvest intervals (PHI) are 7 days, except for flowers (ornamentals), which has none.

a. Application rate for all crops: 0.000064 kg a.i./1L container / 18.6 m^2 = 0.344 µg a.i./cm^2 = 34.4g a.i./ha
b. Transfer coefficients: *Transfer Coefficients for Residential Outdoor Ornamentals and Gardening*, 6 October 2008; *Transfer Coefficients for Orchard Tree Crops and Christmas Trees*, 22 January 2004; Transfer coefficient values (whole body exposure of adult) were adjusted for average body surface area of youth (10–12 years old: 12 700 cm^2), compared to adults (18 440 cm^2).

Table 13 Residential Aggregate Exposure for Adult, Youth and Children to Acetamiprid Residues

Sub-population (age range in years)	Dermally adsorbed systemic dose (mg/kg bw/day)	Inhalation Exposure (mg/kg bw/day)	Dermal exposure (mg/kg bw/day)	Chronic dietary (mg/kg bw/day)	Aggregate [b] exposure (mg/kg bw/day)	Total MOE [c,d] (target = 300)
	M/L/A	M/L/A	Post-application			
Adults (20–49)	9.63×10^{-6}	0.071×10^{-6}	0.0015	1.75×10^{-4}	1.68×10^{-3}	1484
Youth (10–12) [e]	Not applicable	Not applicable	0.0018	2.59×10^{-4}	2.06×10^{-3}	1214
Child (1–6)	Would not be involved in the spraying, and would not participate significantly in activities where crops have been treated. Therefore, exposure was not quantified.					

a. From the dietary exposure assessment values were presented as highly refined, daily chronic food + water background exposure (mg/kg bw/day).
b. Aggregate exposure is the sum of dermal (from RTU applicator and postapplicator scenarios, as appropriate), inhalation (from RTU application), and active-specific, chronic dietary (from food and water) exposures.
c. The offspring NOAEL of 2.5 mg/kg bw/day, from the rat DNT study, was determined to be most protective of the acute dietary and short-term dermal and inhalation exposure. The target MOE (uncertainty factor) associated with this study is 300.
d. MOE calculated according to Science Policy Notice SPN2003-04.
e. Chronic dietary (food and water) value of children 7–12 years old.

Table 14 Aggregate Exposure for Adult, Youth and Children Bystanders Performing Pick-your-own Hand Harvesting and Eating Pome Fruit (Represented by Apples) on the Same Day

Sub-population (age range in years)	Dermally absorbed systemic dose (mg/kg bw/day)	Dietary (mg/kg bw/day)			Aggregate [c] Exposure (mg/kg bw/day)	Total MOE [d,e] (target = 300)
		Acute [a]	Chronic [b]	Total		
General population	0.001	2.24×10^{-3}	2.31×10^{-4}	2.47×10^{-3}	3.47×10^{-3}	720
Adults (20-49)	0.001	1.16×10^{-3}	1.75×10^{-4}	1.34×10^{-3}	2.34×10^{-3}	1071
Youth (10-12) [f]	0.0012	2.28×10^{-3}	2.59×10^{-4}	2.54×10^{-3}	3.74×10^{-3}	669
Child (6-9) [g]	0.0013	3.53×10^{-3}	4.98×10^{-4}	4.03×10^{-3}	5.33×10^{-3}	469
Child (1-6)	0.0019	4.86×10^{-3}	$\mathbf{5.37 \times 10^{-4}}$	$\mathbf{5.40 \times 10^{-3}}$	7.30×10^{-3}	343

a. From the dietary exposure assessment, using the United States maximum field trial residue for apples of 0.64 ppm, food-only, commodity-specific (apple) values presented as a one-day exposure (mg/kg bw/day).
b. From the Dietary Exposure Assessment values were presented as highly refined, daily chronic food + water background exposure (mg/kg bw/day).
c. Aggregate exposure is the sum of dermal (from U-pick), acute dietary (commodity-specific) and chronic dietary (from food and water) exposures.
d. The offspring NOAEL of 2.5 mg/kg bw/day, from the rat developmental neurotoxicity study, was determined to be most protective of the acute dietary and short-term dermal and inhalation exposure. The target MOE is 300.
e. MOE calculated according to Science Policy Notice SPN2003-04.
f. Chronic dietary (food and water) value of children 7–12 years.
g. Chronic dietary (food and water) value of children 3–5 years.

Table 15 Integrated Food Residue Chemistry Summary

Nature of the Residue in Plant and Animal Matrices
Please refer to Regulatory Note REG2002-05 for further information.
Confined Rotational Crop Study
The petitioner was requested to submit data demonstrating the stability of the metabolic profile in various rotational crop commodities (including radish root and sorghum/wheat grain, as well as a leafy vegetable) for up to 11 months, the maximum storage interval for these commodities. A waiver was submitted to address the deficiency. The waiver stated the storage stability of the metabolic profile in rotational crop commodities was not necessary because: • acetamiprid rapidly degrades in soil and no acetamiprid was found in rotational crop matrices; • the toxicity of the metabolites IM-1-4, IM-0 and IC-0 is low; • the precursor of metabolites has been proposed from the metabolic study (acetamiprid and IM-2-1); • no new information would be gained from conducting the stability studies on metabolites of low toxicity; and • the soil metabolite IM-1-4 was the only significant metabolite and not considered to be a metabolite of toxicological concern. **Evaluation of Waiver** Although metabolite IM-1-4 is a major metabolite in rotational crops, it is considered to be less toxic than acetamiprid. As such, acetamiprid is considered to be the only component in the residue definition for risk assessment purposes. Metabolite IM-1-4 is a soil metabolite identified in mustard leaf (0.016–0.021 ppm) at 30, 60, and 120 days after treatment (DAT). Radish leaf had measurable residues of IM-1-4 (0.023 and 0.033 ppm) only at 30 DAT and 120 DAT; sorghum forage comprised 0.040 and 0.018 ppm at 30 DAT and 60 DAT, respectively. IM-1-4 is not a predominant residue in food items at 30, 60, 120 and 365 DAT. Since maximum residue limits are not needed at this time for rotational crop matrices, there is sufficient information on file with regards to the storage stability of the metabolic profile of interest. The stability of acetamiprid residues has been demonstrated in a variety of crops for up to 12 months. Please refer to REG2002-05 for further information.

Confirmatory Crop Field Trials on Broccoli and Cabbage. For data pertaining to original submission please refer to REG2002-05.	**PMRA # 1117904**

Broccoli and cabbage plants were given five broadcast applications of Assail 70 WP (containing acetamiprid) at a rate of ~55–64 g a.i./ha (total seasonal rate of 296 to 302 g a.i./ha; the current rate for cole crops) and a retreatment interval of seven days (±1 day). Broccoli and cabbage samples were harvested seven days after last application.

The results of the trials show that following treatment with acetamiprid at a target rate of 296 to 302 g a.i./ha and a PHI of seven days, residues of acetamiprid in/on broccoli were 0.022 ppm and 0.0376 ppm and residues of acetamiprid in/on cabbage were <LOQ (<0.01 ppm).

Commodity	**Total Rate (g a.i./ha)**	**PHI (days)**	**Residue Levels (ppm)**			
			n	**Min.**	**Max.**	**HAFT**
Acetamiprid						
Broccoli	296	7	2	0.0222	0.0376	-
Cabbage	302	7	2	<0.01	<0.01	-

Residue Decline	**PMRA # 1117904**
Residue decline studies were not included with the study as it was for confirmatory purposes only. Please refer to REG2002-05 for further information.	
Confirmatory Crop Field Trials on Lettuce and Celery. For data pertaining to original submission please refer to REG2002-05.	**PMRA # 1117902 & 1117903**

Lettuce and celery plants were given five broadcast foliar application of Assail 70 WP (containing acetamiprid) at a rate of ~82–95 g a.i./ha (total seasonal rate of 423 to 436 g a.i./ha; 1.4-fold the current rate for leafy vegetables) and a retreatment interval of seven days (±1 day). Lettuce and celery samples were harvested seven days after last application.

The results of the trials show that following treatment with acetamiprid at a target rate of 423 to 436 g a.i./ha and a PHI of seven days, residues of acetamiprid in/on lettuce were 0.078 ppm and 0.14 ppm and residues of acetamiprid in/on celery were from 0.13 ppm to 0.35 ppm.

Commodity	**Total Rate (g a.i./ha)**	**PHI (days)**	**Residue Levels (ppm)**			
			n	**Min.**	**Max.**	**HAFT**
Acetamiprid						
Lettuce	436	7	2	0.078	0.14	-
Celery	423–429	7	4	0.13	0.35	0.33

Residue Decline	**PMRA # 1117902 & 1117903**
Residue decline studies were not included with the study as it was for confirmatory purposes only. Please refer to REG2002-05 for further information.	
Confirmatory Crop Field Trials on Tomatoes. For data pertaining to original submission please refer to REG2002-05.	**PMRA # 1117906**

Tomatoes were given four air-blast applications of Assail 70 WP (containing the a.i. acetamiprid) at a rate of ~57–62 g a.i./ha (total seasonal rate of 236–242 g a.i./ha; 1.4-fold the current rate for tomatoes) and a retreatment interval of seven days (±1 day). Tomato samples were harvested seven days after last application.

The results of the trials show that following treatment with acetamiprid at a target rate of 240 g a.i./ha and a PHI of seven days, residues of acetamiprid in/on tomatoes were 0.013 ppm to 0.064 ppm.

Commodity	**Total Rate (g a.i./ha)**	**PHI (days)**	**Residue Levels (ppm)**			
			n	**Min.**	**Max.**	**HAFT**
Acetamiprid						
Tomatoes	236–242	6–8	10	0.01	0.064	0.058

Residue Decline	**PMRA # 1117906**
Residue decline studies were not included with the study as it was for confimatory purposes only. Please refer to REG2002-05 for further information.	

Confirmatory Crop Field Trials on Pome Fruit (Apples and Pears). For data pertaining to original submission please refer to REG2002-05.	**PMRA # 1117907 & 1117908**

Apple and pear trees were given four broadcast foliar applications of Assail 70WP (containing acetamiprid) at a rate of 164–176 g a.i./ha (total seasonal rate of 661–687 g a.i./ha; the current rate for pome fruit) and a retreatment interval of 10 to 14 days. Apple and pear samples were harvested seven days after last application.

The results of the trials show that following treatment with acetamiprid at a target rate of 661–687 g a.i./ha and a PHI of seven days, residues of acetamiprid in/on apples were 0.17 ppm and 0.15 ppm and residues of acetamiprid in/on pears were 0.19 ppm and 0.28 ppm.

Commodity	**Total Rate (g a.i./ha)**	**PHI (days)**	**Residue Levels (ppm)**			
			n	**Min.**	**Max.**	**HAFT**
Acetamiprid						
Apples	687	7	2	0.15	0.17	-
Pears	661	7	2	0.19	0.28	-

Residue Decline	**PMRA # 1117907 & 1117908**

Residue decline studies were not included with the study as it was for confirmatory purposes only. Please refer to REG2002-05 for further information.

Confirmatory Crop Field Trials Grapes. For data pertaining to original submission please refer to REG2002-05.	**PMRA # 1117905**

Grapes were given two air-blast applications of Assail 70 WP (containing acetamiprid) at a target rate of 55 g a.i./ha (total seasonal rate of 110 g a.i./ha; the current rate for grapes) and a retreatment interval of 14 days. Grape samples were harvested seven days after last application.

The results of the trials show that following treatment with acetamiprid at the target rate of 110–112 g a.i./ha and a PHI of seven days, residues of acetamiprid in/on grapes were 0.118 ppm–0.173 ppm.

Commodity	**Total Rate (g a.i./ha)**	**PHI (days)**	**Residue Levels (ppm)**			
			n	**Min.**	**Max.**	**HAFT**
Acetamiprid						
Grapes	110	7	4	0.118	0.173	0.152

Residue Decline	**PMRA # 1117905**

Residue decline studies were not included with the study as it was for confimatory purposes only. Please refer to REG2002-05 for further information.

Field Accumulation in Rotational Crops

Please refer to REG2002-05 for further information.

Processed Food and Feed

Please refer to REG2002-05 for further information.

Storage Stability

Please refer to REG2002-05 for further information.

Livestock Feeding

Please refer to REG2002-05 for further information.

Table 16 Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment

Plant Studies			
Please refer to REG2002-05 for further information.			
Animal Studies			
Animals			
Please refer to REG2002-05 for further information.			
Dietary Risk from Food and Water			
	Population	**Estimated Risk % of Acceptable Daily Intake (ADI)**	
		Food Only (Highly Refined)	**Food and Water (Highly Refined)**
Refined chronic non-cancer dietary risk **ADI = 0.008 mg/kg bw/day** **Estimated chronic drinking water concentration = 3.16 µg a.i./L (Level II)**	General population	2	2.9
	All infants (<1 year old)	5.6	**8.4**
	Children 1–2 years old	**7.2**	**8.4**
	Children 3–5 years old	5.1	6.2
	Children 6–12 years old	2.7	3.5
	Youth 13–19 years old	1.5	2.1
	Adults 20–49 years old	1.4	2.2
	Adults 50+ years old	1.8	2.6

Refined acute dietary exposure analysis, 99th percentile **Estimated acute drinking water concentration = 10.99 µg a.i./L (Level II)**	**Population**	**Estimated Risk % of Acute Reference Dose (ARfD)**	
		Highly Refined 99th Percentile Food Only (Probabilistic)	**Highly Refined 99th Percentile Food and Water (Probabilistic)**
ARfD = 0.008 mg/kg bw/day	General population	36.8	41
	All infants (< 1 year old)	73	83.1
	Children 1-2 years old	**88.5**	**95**
	Children 3-5 years old	60.9	66.5
	Children 6-12 years old	35.9	39.4
	Youth 13-19 years old	43.4	47.6
	Adults 20-49 years old	28.8	32.2
	Adults 50+ years old	33.8	36.5
	Females 13–49 years old	30	33.4

Table 17 Summary of Risk Assessment for Non-target Terrestrial and Aquatic Species

Organism	Exposure: test substance	Toxicity endpoint value	Converted Tox endpoint value	EEC	RQ value	Level of concern
Terrestrial Organisms						
Earthworm	Acute: **TGAI** acetamiprid	LC_{50}: 9 mg a.i./kg	$LC_{50} \div 2$ = 4.5 mg a.i./kg	0.19 mg a.i./kg	0.04	Not Exceeded
Vascular plant	Vegetative vigour: **TGAI**	EC_{25} (lettuce): 6.5 g a.i./ha	6.5 g a.i./ha (no conversion)	167.7g a.i./ha	25.8	EXCEEDED
Mallard duck	Reproduction: **TGAI** acetamiprid	NOEC: 125 mg a.i./kg diet	5.2 mg a.i./kg bw/day (see text for conversion)	2.7 mg a.i./kg bw/day	0.52	Not exceeded
Aquatic Organisms						
Freshwater midge	Acute: **TGAI** acetamiprid	LC_{50}: 24 µg a.i./L	$LC_{50} \div 2$ = 12 µg a.i./L	160 µg a.i./L	13.3	EXCEEDED
Freshwater amphipod	Acute: **TGAI** acetamiprid	LC_{50}: 100 µg a.i./L	$LC_{50} \div 2$ = 50 µg a.i./L	160 µg a.i./L	3.2	EXCEEDED
Fish- early life stage	Chronic: **TGAI** acetamiprid	NOEC: 19.2 mg a.i./L	19.2 mg a.i./L (no conversion)	0.16 mg a.i./L	0.008	Not exceeded

Table 18 Alternative Active Ingredients Currently Registered for Uses on the Labels of Pest Control Products Containing Acetamiprid

Pest	Registered Alternative Active Ingredients
Aphids	Carbamates: carbaryl, methomyl, oxamyl, pirimicarb; Organophosphates: acephate, chlorpyrifos, diazinon, dichlorvos, dimethoate, malathion, methamidophos, naled, phosalone, phosmet; Organochlorines: endosulfan; Pyrethroids: d-trans allethrin, lambda-cyhalothrin, deltamethrin, permethrin, d-phenothrin, resmethrin, tetramethrin; Pyrethrins; Neonicotinoids: imidacloprid, thiamethoxam; Nicotine; Juvenile hormone mimics: kinoprene; Selective homopteran feeding blockers: pymetrozine; Tetronic and tetramic acid derivatives: spirotetramat; Mitochondrial electron transport inhibitors: rotenone; Insecticidal soaps: alkanolamine salts of fatty acids, potassium salts of fatty acids; Mineral oil; Diatomaceous earth
Whiteflies	Carbamates: carbaryl, pirimicarb; Organophosphates: acephate, chlorpyrifos, dichlorvos, dimethoate, malathion, naled; Organochorines: endosulfan; Pyrethroids: d-trans allethrin, permethrin, d-phenothrin, resmethrin, tetramethrin; Pyrethrins; Spinosyns: spinosad; Juvenile hormone mimics: kinoprene, pyriproxyfen; Selective homopteran feeding blockers: pymetrozine; Tetronic and tetramic acid derivatives: spiromesifen, spirotetramat; Mitochondrial electron transport inhibitors: pyridaben; Insecticidal soaps: alkanolamine salts of fatty acids, potassium salts of fatty acids; Mineral oil

Pest	Registered Alternative Active Ingredients
Colorado potato beetle	Carbamates: carbaryl, carbofuran, oxamyl; Organophosphates: acephate, chlorpyrifos, diazinon, malathion, methamodiphos, phosmet; Organochlorines: endosulfan; Pyrethroids: lambda-cyhalothrin, cypermethrin, deltamethrin, permethrin; Pyrethrins; Neonicotinoids: imidacloprid, thiamethoxam; Spinosyns: spinosad; Microbials: *Bacillus thuringiensis* subsp. *tenebrionis*; Benzoylureas: novaluron; Moulting disruptors: cyromazine; Mitochondrial electron transport inhibitors: rotenone; Ryanodine receptor modulators: chlorantraniliprole; Mineral oil; Diatomaceous earth
Tentiform leafminers	Carbamates: carbaryl, methomyl, oxamyl; Organophosphates: diazinon, phosmet; Pyrethroids: lambda-cyhalothrin, cypermethrin, deltamethrin, permethrin; Neonicotinoids: imidacloprid, thiacloprid, thiamethoxam; Spinosyns: spinetoram; Chloride channel activators: abamectin; Moulting disruptors: methoxyfenozide, tebufenozide; Ryanodine receptor modulators: chlorantraniliprole
Leafhoppers	Carbamates: carbaryl, carbofuran, formetanate, methomyl, oxamyl, pirimicarb; Organophosphates: acephate, azinphos-methyl, chlorpyrifos, diazinon, dimethoate, malathion, methamidophos, naled, phosalone, phosmet; Organochlorines: endosulfan; Pyrethroids: d-trans allethrin, lambda-cyhalothrin, cypermethrin, deltamethrin, permethrin, d-phenothrin, tetramethrin; Pyrethrins; Neonicotinoids: imidacloprid, thiacloprid, thiamethoxam; Mitochondrial electron transport inhibitors: rotenone; Insecticidal soaps: potassium salts of fatty acids; Mineral oil; Diatomaceous earth; Kaolin clay
Codling moth	Carbamates: carbaryl, methomyl; Organophosphates: azinphos-methyl, diazinon, malathion, phosalone, phosmet; Organochlorines: endosulfan; Pyrethroids: lambda-cyhalothrin, cypermethrin, deltamethrin, permethrin; Neonicotinoids: thiacloprid; Spinosyns: spinetoram, spinosad; Benzoylureas: novaluron; Moulting disruptors: methoxyfenozide, tebufenozide; Ryanodine receptor modulators: chlorantraniliprole; Microbials: *Cydia pomonella* granulosis virus; Kaolin clay; Pheromones: E,E-8,10-dodecadien-1-ol + 1-dodecanol + 1-tetradecanol
Pear psylla	Carbamates: carbaryl; Organophosphates: azinphos-methyl, diazinon, dimethoate, malathion, phosalone, phosmet; Organochlorines: endosulfan; Pyrethroids: lambda-cyhalothrin, cypermethrin, deltamethrin, permethrin; Pyrethrins; Neonicotinoids: thiamethoxam; Chloride channel activators: abamectin; Tetronic and tetramic acid derivatives: spirotetramat; Mitochondrial electron transport inhibitors: pyridaben; Insecticidal soaps: potassium salts of fatty acids; Mineral oil; Kaolin clay
European pine sawfly	Organophosphates: acephate, chlorpyrifos
Swede midge	Pyrethroids: lambda-cyhalothrin

Pest	Registered Alternative Active Ingredients
Oriental fruit moth on pome fruits	Pyrethroids: deltamethrin; Neonicotinoids: thiacloprid; Spinosyns: spinetoram; Benzoylureas: novaluron; Moulting disruptors: methoxyfenozide; Ryanodine receptor modulators: chlorantraniliprole; Kaolin clay; Pheromones: Z-8-dodecen-1-yl acetate + E-8-dodecen-1-yl acetate + Z-8-dodecen-1-ol
Pea leafminer	Chloride channel activators: abamectin; Moulting disruptors: cyromazine

Appendix II Supplemental Maximum Residue Limit Information—International Situation and Trade Implications

Health Canada's List of MRLs under the *Pest Control Products Act*.

Table 1 Differences Between Canadian MRLs and Other Jurisdictions

Commodity	Canada	United States	Codex*
Meat byproducts of cattle, hogs, horses, goats, sheep	0.3 ppm	0.2 ppm	-

* Codex is an international organization under the auspices of the United Nations that develops international food standards, including MRLs.

MRLs may vary from one country to another for a number of reasons, including differences in pesticide use patterns and the locations of the field crop trials used to generate residue chemistry data. For animal commodities, differences in MRLs can be due to different livestock feed items and practices.

Under the North American Free Trade Agreement, Canada, the United States and Mexico are committed to resolving MRL discrepancies to the broadest extent possible. Harmonization will standardize the protection of human health across North America and promote the free trade of safe food products. Until harmonization is achieved, the Canadian MRLs specified in this document are necessary. The differences in MRLs outlined above are not expected to impact businesses negatively or adversely affect international competitiveness of Canadian firms or to negatively affect any regions of Canada.

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

PMRA Document Number: 1117945
Reference: 2002, Dissociation Constant of IM-1-5, Data Numbering Code: 2.14.10

PMRA Document Number: 1117901
Reference: 2005, Assail 70 WP Insecticide; Two Year Storage Stability and Corrosion Characteristics, Data Numbering Code: 3.5.10

PMRA Document Number: 1526781
Reference: 2007, Acetamiprid 50 FS: Storage Stability and Corrosion Characteristics, Data Numbering Code: 3.5.10

PMRA Document Number: 1117798
Reference: 2005, Two Year Storage Stability and Corrosion Characteristics -10.3.2- An All Inclusive Report, Data Numbering Code: 3.5.10

2.0 Human and Animal Health

PMRA Document Number: 1117902
Reference: 2003, Determination of Acetamiprid Residues in Mature Lettuce Following Foliar Applications with Assail, BCS03-03, Data Numbering Code: 7.4.1

PMRA Document Number: 1117903
Reference: 2003, Determination of Acetamiprid Residues in Mature Celery Following Foliar Applications with Assail, BCS03-05, Data Numbering Code: 7.4.1

PMRA Document Number: 1117904
Reference: 2004, Acetamiprid: Magnitude of Residues in Broccoli and Cabbage Following Foliar Applications with Assail 70WP, NIS03103, Data Numbering Code: 7.2.1,7.4.1

PMRA Document Number: 1117905
Reference: 2004, Acetamiprid: Magnitude of Residues in grape Following Foliar Applications with Assail 70WP, NIS03102, Data Numbering Code: 7.2.1,7.4.1

PMRA Document Number: 1117906
Reference: 2004, Acetamiprid: Magnitude of Residues in Tomatoes Following Foliar Applications with Assail 70WP, NIS03101, Data Numbering Code: 7.2.1,7.4.1

PMRA Document Number: 1117907
Reference: 2003, Determination of Acetamiprid Residues in Mature Apples Following Foliar Applications with Assail, BCS03-02, Data Numbering Code: 7.4.1

PMRA Document Number: 1117908
Reference: 2003, Determination of Acetamiprid Residues in Mature Pears Following Foliar Applications with Assail, BCS03-04, Data Numbering Code: 7.4.1

PMRA Document Number: 1117909
Reference: 2005, NI-25 (Acetamiprid) Consideration of the Storage Stability in Confined Crop Rotational Study of Acetamiprid, Data Numbering Code: 7.4.3

PMRA Document Number: 1117941
Reference: 2002, Acetamiprid Waiver Request for Radiovalidation for IM-2-1 Amide, AC02-19, Data Numbering Code: 7.2.3

PMRA Document Number: 1449434
Reference: 2007, Percent Human Dermal Absorption for Acetamiprid, Data Numbering Code:4.3.8, 5.8

PMRA Document Number: 1453764
Reference: 2007, Acetamiprid Dermal Absorption Rate for Use in Occupational Risk Assessments, Data Numbering Code: 4.3.8

PMRA Document Number: 1117946
Reference: 2002, IM-1-5: Acute Oral Toxicity Study in Rats, H220, Data Numbering Code 4.2.1.

PMRA Document Number: 1117947
Reference: 2002, Acetamiprid Suspended in Corn Oil: Acute Oral Toxicity Study in Rats, H221, Data Numbering Code 4.2.1.

PMRA Document Number: 1117948
Reference: 2003, Metabolism Study of Acetamiprid in Rat (Determination of IM-1-5), NSM02-024, Data Numbering Code 4.5.9.

PMRA Document Number: 1117940
Reference: 2003, An Oral Developmental Neurotoxicity Study of Acetamiprid in Rats. WIL-21193, Data Numbering Code 4.5.14.

PMRA Document Number: 1357277
Reference: 2006, Rebuttal of Data Evaluation Record for Acetamiprid, 21193, Data Numbering Code 4.5.14.

PMRA Document Number: 1449435
Reference: 2007, Acetamiprid DNT Study: NOAEL & LOAEL Evaluation (with explanatory notes added), EPA OPP HED Meeting, Data Numbering Code 4.5.14.

PMRA Document Number: 1453765
Reference: 2007, Characterization of Critical Toxicology Endpoints for Acetamiprid Risk Assessment: Auditory Startle Habituation and Maternal Toxicity from the Developmental Neurotoxicity Study, Data Numbering Code 4.5.14.

PMRA Document Number: 1449436
Reference: Non-GLP Statistical Analysis Conducted by Exponent, Inc. Acetamiprid DNT Study WIL-21193 MRID 46255619. Data Numbering Code 4.5.14.

PMRA Document Number: 1470632
Reference: 2007, Acetamiprid DNT Study (WIL-21193; MRID 46255619): Response to EPA CEB Statistical Analyses and Weight of Evidence Supporting NOAEL of 10 mg/kg bwt/day, Data Numbering Code 4.5.14.

3.0 L. ment

PMRA Document Number: 1117942
Reference: 2003, Position statement on persistence and mobility of IM-1-5 in soil, Data Numbering Code 8.5.

PMRA Document Number: 1117944
Reference: 2003, 14C Acetamiprid: aged residue column leaching study in two calcareous soils, CX02018, RD-03103, Data Numbering Code 8.2.4.3.2.

PMRA Document Number: 1117943
Reference: 2002, 14C Acetamiprid: rate of degradation in three calcareous soils at 20 °C, CX01013, RD-00168, Data Numbering Code 8.2.3.4.2.

PMRA Document Number: 1117945
Reference: 2002, Dissociation constant of IM-1-5, NCAS 02-132, Data Numbering Code 2.14.10.

PMRA Document Number: 1117957
Reference: 2003, Position paper on persistence of IM-1-4 in sediment, RD-03199, Data Numbering Code 8.5.

PMRA Document Number: 1117958
Reference: 2003, Position paper on IB-1-1, RD-03200, Data Numbering Code 8.5.

PMRA Document Number: 1117960
Reference: 1998, Evaluation of toxicity of residues of acetamiprid (NI-25) on alfalfa to honey bee (Apis mellifera), 98-1-7214, RD-03115, Data Numbering Code 9.2.4.

PMRA Document Number: 1117961
Reference: 2003, Acute contact and oral toxicity of EXP60707A to the bumblebee Bombus terrestris L. under laboratory conditions, 20021 073102-BLEU, Data Numbering Code 9.2.4.

PMRA Document Number: 1117962
Reference: 2002, A semi-field study on the effects on honey bees (Apis mellifera L.) of ASSAIL 70 WP (EXP61842A, Acetamiprid 70%) Straight and in Combination with the Fungicide PROCURE 50WS (Triflumizole 50%), 20011239/SI-BZEU, Data Numbering Code 9.2.4.

PMRA Document Number: 1117951
Reference: 2002, IM-1-5: acute toxicity to Daphnia magna, NCAS 01-197, RD-11 02414, Data Numbering Code 9.3.2.

PMRA Document Number: 1117965
Reference: 2003, Acetamiprid Technical - Acute Toxicity to Midge (Chironomus riparius) Under Static Conditions, 12681.6104, Data Numbering Code 9.3.4.

PMRA Document Number: 1117964
Reference: 2003, Acetamiprid Technical - Acute Toxicity to Gammarids (Gammarus fasciatus) Under Static Conditions, Data Numbering Code 9.3.4.

PMRA Document Number: 1117969
Reference: 2003, Acetamiprid - Determination of Effects on Vegetative Vigour of Lettuce (Lactuca sativa), 02571-1075, 12681/6107, Data Numbering Code 9.8.4.

PMRA Document Number: 1117967
Reference: 2000, Acetamiprid: A Reproduction Study with the Northern Bobwhite, 437-104, Data Numbering Code 9.6.3.1.

PMRA Document Number: 1117968
Reference: 2004, Acetamiprid (NI-25) - Reproductive Toxicity Test with Mallard Duck (Anas platyrhynchos), 13798.4105. Data Numbering Code 9.6.3.2.

4.0 Value

PMRA Document Number: 1117802
Reference: 2004, Control of European pine sawfly in Scotch pine with Tristar, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117803
Reference: 2005, Control of European pine sawfly in Scotch pine, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117916
Reference: 2005, Control of green peach aphid on tomato, Trial 1, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117917
Reference: 2005, Control of green peach aphid on tomato, Trial 2, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117918
Reference: 2005, Control of green apple aphid on red delicious apple, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117919
Reference: 2005, Control of green apple aphid on empire apple, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117920
Reference: Minimum effective rate of Assail against aphid pests of apple, Trial 1, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117921
Reference: Minimum effective rate of Assail against aphid pests of apple, Trial 2, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117922
Reference: 2003, Evaluation of Assail for control of aphids in lettuce, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117923
Reference: 2002, Evaluation of Assail for control of aphids in cauliflower, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117924
Reference: 2003, Evaluation of Assail for control of aphids in cauliflower, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117925
Reference: 2001, Control of first generation spotted tentiform leafminer, mullein leaf bug, and rosy apple aphid on apple, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117926
Reference: 2001, Control of first generation spotted tentiform leafminer and mullein leaf bug on apple with various insecticides, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117927
Reference: 2001, Assessment of insecticides for control of pear psylla and plum curculio on pear, Data Numbering Code 10.2.3.3

PMRA Document Number: 1117928
Reference: 2002, Control of pear psylla on pear with insecticides, Data Numbering Code 10.2.3.3

B. Additional Information Considered

I) Published Information

1.0 Human and Animal Health

Ajarem, J.S. and Ahmad, M. (1998). Prenatal nicotine exposure modifies behavior of mice through early development. Pharmacology Biochemistry and Behavior, 59:313-318.

Banerjee, T.D., Middleton, F., Faraone, S.V. (2007). Environmental risk factors for attention-deficit hyperactivity disorder. Acta Paediatrica 96:1269-1274.

Dwyer, J.B., Broide, R.S, Leslie, F.M. (2008). Nicotine and brain development. Birth Defects Res. C. Embryo Today, 84:30-44.

Levin, E.D., Briggs, S.J., Christopher, N.C., Rose, J.E. (1993). Prenatal nicotine exposure and cognitive performance in rats. Neurotoxicology and Teratology, 15:251-260.

Liang, K., Pytress, B.S., Chen, Y., Leslie, F.M., Weinberger, N.M., Metherate, R. (2006). Neonatal nicotine exposure impairs nicotinic enhancement of central auditory processing and auditory learning in adult rats. Eur. J. Neurosci. 24:857-866.

Shacka, J.J., Fennell, O.B., Robinson, S.E. (1997). Prenatal nicotine sex-dependently alters agonist-induced locomotion and stereotypy. Neurotoxicology and Teratology, 19:167-176.

Slikker, W. Jr., Xu, Z. A., Levin, E.D., Slotkin, T.A. (2005). Mode of action: Disruption of brain cell replication, second messenger, and neurotransmitter systems during development leading to cognitive dysfunction – developmental neurotoxicity of nicotine. Critical Reviews in Toxicology, 35:703-711.

Slotkin, T.A. (1998). Fetal nicotine or cocaine exposure: which one is worse? J. Pharmacol. Exp. Ter. 285:931-945.

Thomas, J.D., Garrison, M.E., Slawecki, C.J., Ehlers, C.L., Riley, E.P. (2000). Nicotine exposure during the neonatal brain growth spurt produces hyperactivity in preweanling rats. Neurotoxicology and Teratology, 22:695-701.

Vaglenova, J., Birru, S., Pandiella, N.M., Breese, C.R. (2004). An assessment of the long-term developmental and behavioral teratogenicity of prenatal nicotine exposure. Behavioural Brain Research, 150: 159-170.

2.0 Environment

Iwasa T., Motoyama N., Ambrose J.T., Roe R.M. 2004. Mechanism for the differential toxicity of neonicotinoid insecticides in the honey bee, *Apis mellifera. Crop Protection* 23: 371–378.